RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

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Pulmonary Complications of Acute Bulbar Poliomyelitis[1]

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MANY OF THE DEATHS in acute bulbar poliomyelitis have been attributed to pulmonary complications, among which are listed suppurative tracheobronchitis, pneumonia, atelectasis, mediastinal emphysema, and pneumothorax. The literature so far encountered, however, fails to reveal any report correlating these lesions, roentgenologically demonstrated, with the clinical course of the disease. This study was undertaken to evaluate, if possible, the various pulmonary complications and to alert clinicians and radiologists to the possible factors which predispose to their development.

It has been observed by many (2, 4, 7, 15, 17) that symptoms of cerebral involvement in bulbar poliomyelitis, heretofore considered a result of actual virus infection, have cleared completely almost immediately after establishment of an unobstructed airway. Thus, the treatment and prevention of pulmonary acidosis and anoxia (1) have emerged as a most vital adjunct to therapy. Histopathologic studies reported by Courville (3) emphasize that it is extremely difficult to differentiate the pathological changes produced by the virus from those due solely to anoxia. This lends further emphasis to the need for the prevention of pulmonary acidosis and the maintenance of proper oxygenation of the central nervous system.

There are two phases during which the absence of a free respiratory exchange of gases presents itself as a definite threat to the life of the patient with bulbar poliomyelitis (4). The first, or ventilatory phase, occurs during the early days of the disease, when respiratory muscular paralysis, laryngeal paralysis or spasm, and pharyngeal paralysis with secretional obstruction are presenting features. Here the signs of acidosis and oxygen lack are obvious and the symptoms dramatic. The second, or alveolar phase, occurs later, when pulmonary complications develop. During this period the changes are more insidious and persistent and, if unrecognized, frequently lead to death.

The pathogenesis of acidosis and anoxia early in poliomyelitis depends upon an interesting series of events, many of which are etiologic factors in producing pulmonary complications. Pharyngeal paralysis, due to involvement of the 5th, 9th, 10th, 11th, and 12th cranial nerves, together with hypersecretion, which occurs commonly in these patients, results in the accumulation and pooling of secretions in the hypopharynx. With each respiratory cycle, the secretion may overflow into the

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Fig. 1. Roentgen examination of the chest. The patient has been temporarily removed from the body of the respirator. The metal headpiece of the respirator remains in place and obscures the upper portion of the thorax.

trachea or, in those cases in which a respirator is used, may actually be sucked into the tracheobronchial tree.

There are, however, other factors which lead to these changes. Acute obstruction of the larynx is not uncommonly produced by laryngeal paralysis but is more frequently caused by adductor spasm resulting from irritation by secretions. In addition, secretions frequently are retained in the tracheobronchial tree due to ineffectiveness of the cough reflex as a result of muscular paralysis. This not only causes mechanical obstruction but also inflammatory pulmonary disease. There is considerable evidence showing that a tracheotomy which by-passes the obstruction and allows removal of the contaminated secretions prevents this type of anoxia (8, 9, 11, 13, 15, 17). Thus, the ventilatory phase of anoxia is well understood and methods by which it can be prevented and treated are well outlined. This is not true of the alveolar type. It is hoped that this study will contribute to a better understanding of that phase, its prevention and treatment.

MATERIAL

Of 1,119 patients with poliomyelitis admitted to the Contagious Disease Unit of the Los Angeles County Hospital during 1949, 208 had bulbar symptoms. Fifty-three of these (25 per cent) were chosen for this study. The choice was made from a random list of approximately one-half of all the cases of bulbar poliomyelitis, solely on the basis of having had one or more roentgen examinations of the chest. Because these roentgenograms were obtained when pulmonary complications were suspected clinically, our observations may be weighted. Also, this study has been limited in that it does not include complications which may have occurred after transfer of the patient to a secondary hospital.

Roentgen examination of the chest of a patient confined to a respirator is a difficult procedure. As illustrated in Figure 1, the respirator is opened and the patient, with metal headpiece attached, is rolled out of the body of the respirator itself. The bedside x-ray unit then is centered properly and a cassette is placed beneath the patient's thorax. The following exposure factors are employed: 32-inch tube-film distance, 70 kv., 15 ma., and 0.1 to 0.3 seconds exposure, depending on the thickness of the thorax.

The roentgenograms are made with the patient in the supine position. The metal headpiece of the respirator usually prevents adequate visualization of the apices. Often the patient's condition makes proper positioning difficult. In most cases the muscles of respiration are partially or completely paralyzed so that some form of artificial respiration must be maintained during the examination. Therefore, a physician must be in attendance. The entire procedure must be carried out rapidly and with as little disturbance to the patient as possible.

CLINICAL OBSERVATIONS

The 53 patients studied were divided into two groups, 31 (58 per cent) with and 22 (42 per cent) without roentgen evidence of pulmonary complications. These two groups were then compared as to age, sex, race, duration of symptoms before admission to the hospital, difficulty in swallowing, paralysis of the diaphragm and inter-

TABLE I: CORRELATION OF AGE WITH PULMONARY COMPLICATIONS

Age	0–1	2–5	6–10	11–15	16–20	21–30	31–40	41–50
With pulmonary complications	2	4	3	3	4	11	1	3
Without pulmonary complications	0	1	6	3	2	6	2	2

costal muscles, secretions, temperature, initial white blood count, vomiting, time of entry to respirator, time of tracheotomy, and amount of intestinal gas.

Age: Age appears to be an important factor only in patients of less than six years, where pulmonary complications occurred in 6 out of 7 cases. The lumen of the tracheobronchial tree before the age of six, and particularly in patients under two years of age, is so small that almost any swelling of the mucous membrane is sufficient to cause a complete or partial obstruction. This and the readiness with which the tracheobronchial mucosa becomes edematous in response to trauma and infection explain the increased susceptibility of children. While there were only 2 patients in this series below one year of age, the fact that both had pulmonary lesions and died serves only to emphasize the seriousness of bulbar poliomyelitis complicated by pulmonary disease in the very young.

Sex: The patients included in this study were divided almost evenly as to sex, 28 females and 25 males. Pulmonary complications, however, developed in almost twice as many females as males, 20 females as compared to 11 males. Notwithstanding this, 6 of the 7 patients who died were males. This disproportionately high death rate among the male patients is not due entirely to our sampling of cases. Of the 21 fatalities in the entire group of 208 patients admitted in 1949 with bulbar poliomyelitis, 16 were in males.

Atelectasis, which apparently was the most serious of the pulmonary lesions, since it was present in all of those who died, occurred in 13 females as compared to 9 males. The higher mortality in males with bulbar poliomyelitis cannot be explained, therefore, by the incidence or severity of the pulmonary complications which may be present. Perhaps the male is more susceptible to the acidosis and anoxia which almost invariably accompany these lesions. The respirator, acting primarily on the thoracic cage, may be a more physiological form of artificial respiration for the female, whose respiration is chiefly thoracic, than for the male, whose respiration is chiefly abdominal.

Race: All of the patients were Caucasians.

Duration of Symptoms Before Admission: Most of the patients in both groups entered the hospital five days or less after the onset of symptoms. The incidence of pulmonary complications apparently was not related to the duration of symptoms prior to admission.

TABLE II: CORRELATION OF DURATION OF SYMPTOMS WITH PULMONARY COMPLICATIONS

Duration of Symptoms Before Admission (days)	1	2	3	4	5	6	7	8	9	10	11	12	13
With pulmonary complications	1	4	8	7	5	1	2	0	1	1	0	0	1
Without pulmonary complications	1	4	3	3	5	2	2	2	0	0	0	0	0

Temperature: On admission, most patients were febrile, with temperatures ranging up to 105.6°. Usually the temperature reached a peak within several days and then subsided by lysis. Two patients in whom pulmonary complications developed and 4 others were afebrile on admission and throughout their stay in the hospital. There was no significant difference in either the initial or peak temperatures of the two groups.

TABLE III: CORRELATION OF DYSPHAGIA AND RESPIRATORY MUSCULAR PARALYSIS WITH PULMONARY COMPLICATIONS

	Difficulty in Swallowing				Paralysis of Diaphragm				Paralysis of Intercostal Muscles			
	0	+	++	+++	0	+	++	+++	0	+	++	+++
With pulmonary complications	3	8	8	12	8	8	8	7	7	5	7	12
Without pulmonary complications	3	3	6	10	6	11	2	3	5	6	2	9

Initial White Blood Count: The white blood counts on admission varied from 8,000 to 36,200, with no significant difference apparent in those in whom pulmonary complications did or did not develop. Secondary rises in temperature and white blood count were frequently associated with pulmonary complications and in other instances were accounted for by urinary tract infections, otitis media, and other inflammatory lesions.

Vomiting: Vomiting occurred frequently before admission but only occasionally during the hospital stay. While aspiration of gastric contents may have been the cause of some of the pulmonary lesions, the incidence of vomiting was so similar in both groups that no significant relationship to the development of pulmonary complications was apparent.

Difficulty in Swallowing; Paralysis of Diaphragm and Intercostal Muscles: These findings were graded from 0 to +++ depending on the degree of loss of function, with 0 representing normal and +++ complete loss of function (Table III).

The incidence or severity of dysphagia and paralysis of the diaphragm or intercostal muscles showed no correlation with the presence or absence of pulmonary complications. This was so in spite of the fact that paralysis of the swallowing mechanism leads to pooling of secretions, and paralysis of the respiratory muscles reduces the efficiency of the cough reflex. Both of these factors are largely responsible for secretional obstruction.

Secretions: The amount of combined nasal, pharyngeal, and tracheobronchial secretions of each patient was estimated as being minimal, moderate, or marked. The thought has been repeatedly expressed that the accumulation of secretions in the respiratory passages, by producing an obstruction to the airway and subsequent asphyxia, furnishes the most important threat to the life of the patient (2, 7, 8, 10, 14, 17). Hypersecretion is a part of the pathologic physiology of bulbar poliomyelitis (8, 13). It occurs early in the disease and precedes the development of pulmonary complications. Normally, 1,000 to 1,500 c.c. of saliva are secreted daily, whereas in patients with bulbar poliomyelitis more than 2,000 c.c. of saliva have been recovered (7). As might have been expected, Table IV indicates that the incidence of pulmonary complications was highest in those who had the largest amount of secretions.

TABLE IV: CORRELATION OF SECRETIONS WITH PULMONARY COMPLICATIONS

	Minimal	Moderate	Marked
With pulmonary complications	2	5	24
Without pulmonary complications	5	4	13

In all patients the secretions obtained from the tracheobronchial tree became thick and purulent after a period of time. Actual tracheal and bronchial plugs were aspirated rather frequently from those in

TABLE V: CORRELATION OF PULMONARY COMPLICATIONS WITH TIME OF ENTRY TO RESPIRATOR AFTER ADMISSION

Day of Hospitalization	1	2	3	4	5	6	7	8	9	10
With pulmonary complications	14	10	2	3	0	0	0	0	0	1
Without pulmonary complications	7	7	2	1	3	0	1	0	0	0

TABLE VI: CORRELATION OF PULMONARY COMPLICATIONS WITH TIME OF TRACHEOTOMY

Day of Hospitalization	1	2	3	4	5	6	7	8	9	10	11	16	60	90
With pulmonary complications	7	9	3	3	1	1	0	1	2	0	1	1	1	1
Without pulmonary complications	9	5	2	0	0	2	1	1	0	0	0	0	0	0

whom pulmonary complications occurred and infrequently from those without pulmonary involvement.

Time of Entry to Respirator: The average time between admission and entry to the respirator was approximately the same for the two groups. Eventually all but one patient in each group were placed in a respirator.

Tracheotomy: All patients with pulmonary complications and 20 of the 22 patients without had a tracheotomy. In both groups tracheotomy was done in a majority of cases on the first or second day of hospitalization.

TABLE VII: CORRELATION OF PULMONARY COMPLICATIONS WITH TIME INTERVAL BETWEEN TRACHEOTOMY AND ENTRY TO RESPIRATOR

	With Pulmonary Complications	Without Pulmonary Complications
Placed in respirator on day of tracheotomy	14	12
Placed in respirator at least 1 day before tracheotomy	13	4
Placed in respirator at least 1 day after tracheotomy	3	3
Tracheotomy but not placed in respirator	1	1
Placed in respirator but did not have tracheotomy	0	2

The interval of time between the placing of a patient in a respirator and the performance of a tracheotomy appears to be particularly significant, though the average time after admission that a patient was placed in a respirator (Table V) or had a tracheotomy (Table VI) was not notably different in the two groups. Table VII indicates that of patients who underwent tracheotomy one or more days before entering the respirator, approximately equal numbers did and did not have pulmonary complications. On the other hand, pulmonary lesions developed in 13 out of 17 patients who entered respirators one or more days before the performance of tracheotomy. The two patients in whom tracheotomy was not done and in whom no pulmonary complications occurred had only a minimal amount of secretions. In 6 of the 7 fatal cases, tracheotomy was performed one or more days after the patient had been placed in a respirator. Three had a tracheotomy sixteen, sixty, and ninety days respectively after they were placed in a respirator, and then only after the development of sudden respiratory distress. These findings are consistent with the concept that, unless the secretions which accumulate in the upper air passages are by-passed by a tracheotomy, the negative pressure of the respirator may draw some of these secretions distally, resulting in the production of bronchial obstruction (7, 11, 13).

Intestinal Gas: Most patients had more intestinal gas than might be expected ordinarily. Mild to moderate gastric distention was particularly common. This may be attributed to aspiration of air through the esophagus and disturbance of gastro-intestinal motility secondary to dysfunction of the autonomic nervous system. We have no evidence that the intestinal distention of the average patient was directly responsible for any of the pulmonary lesions. However, it is known that any significant distention limits diaphragmatic movement and reduces vital capacity.

Acute, sudden gastric dilatation in any patient with impaired respiratory function constitutes a serious hazard to life. In 3 of the 4 patients in this series who had acute gastric dilatation pulmonary complications developed simultaneously. In the other, a thirty-eight-year-old female, epigastric distress and abdominal distention ensued seventeen days after admission and lasted for approximately six weeks. Intermittent gastric suction by means of a Levine tube gave temporary relief. Finally an

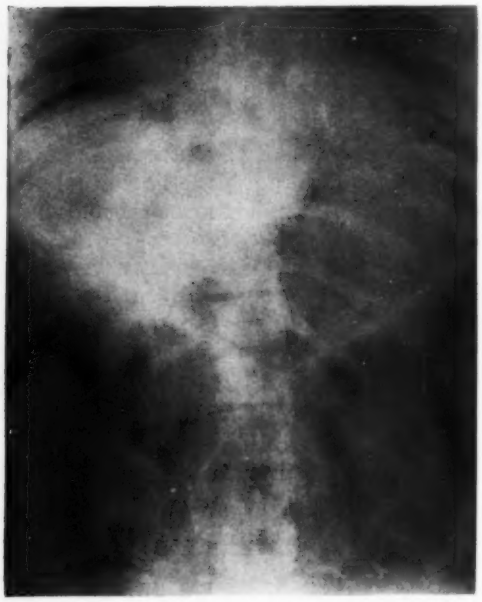


Fig. 2. Acute gastric dilatation; atelectasis with superimposed infection. J. C. T., male, age 21, admitted July 30, 1949, with acute bulbar spinal poliomyelitis, one day after onset of symptoms. Slight weakness of diaphragm and intercostal muscles. Moderate dysphagia. Placed in respirator one day after admission. Tracheotomy four days later because of respiratory difficulty and increasing amount of secretions. Complained of abdominal distention. Clinical diagnosis of acute gastric dilatation made on Aug. 1, Aug. 2, and Aug. 6. On Aug. 6, 600 c.c. of fluid and 400 c.c. of air removed from stomach by Levine tube suction, which had been used intermittently since Aug. 1. Temperature on admission 102°, gradually rising to 104.8°. Death Aug. 9, 1949.

Roentgenogram of Aug. 6, 1949. Lung fields incompletely visualized. Atelectasis of right lower lobe. Moderate gastric dilatation remains after removal of air and fluid as noted above. Gaseous distention of both small and large bowel.

extreme gastric dilatation developed, and 9 quarts of gas were removed from the stomach. Complete relief was obtained by continuous gastric suction. The other 3 cases of gastric dilatation occurred in patients having pulmonary lesions. A six-year-old girl, who recovered, had an associated minimal right upper lobe pneumonia. The remaining two patients died with associated atelectasis. In one, a five-month-old male, acute gastric dilatation and atelectasis of the left lung developed three months after entry; the other, a twenty-one-year-old male, had gastric dilatation beginning one day after admission, with atelectasis of the right lower lobe (Fig. 2).

The prolonged use of a gastric tube for either feeding purposes or suction may produce local irritation or electrolyte depletion. The Levine tube also has been objected to on the grounds that air can be aspirated through it rather easily (7).

It was noted consistently, however, that in none of those in whom a gastric tube was used continuously did a significant amount of gas occur in either the stomach or the remainder of the intestinal tract. Abnormal quantities of gas, when present, usually were controlled effectively by gastric suction.

PULMONARY COMPLICATIONS

Thirty-one (58 per cent) of the patients studied had roentgen evidence of one or more pulmonary lesions. Since roentgenograms were obtained only when pulmonary involvement was suspected clinically, this may not represent the true incidence. A number of pulmonary lesions, in the absence of overt clinical manifestations, may have been overlooked. Also, some patients were too ill to permit a roentgen examination.

Roentgenograms were not obtained as early or as frequently as might be desired because of the technical difficulties previously described. Hence, it is not possible to state exactly when pulmonary complications are most likely to occur. For lack of a more accurate method, it was necessary to date the pulmonary lesions from the time they were first demonstrated roentgenologically. From the available data, these lesions appear more likely to occur rather late in the acute illness. They were found one to ninety days after admission to the hospital, the average interval being 14.6 days and the mean eight days. This corresponds to the period when tracheal and bronchial secretions tend to become thick and purulent due to secondary infection.

Most, if not all, of the pulmonary complications encountered can be explained by the various phenomena which follow com-

plete or partial bronchial obstruction by retained or aspirated secretions. There was a relatively high incidence of upper lobe lesions in keeping with the fact that the corresponding bronchi are the most dependent in the supine position in the respirator.

Pneumonia: Lesions were interpreted as being purely inflammatory when there was no roentgen evidence of the contractive manifestations of atelectasis and when there was an accompanying rise in temperature and white blood count.

Nine patients had predominantly patchy pneumonia, tending in some cases to become confluent, and either unilateral or bilateral in distribution. Aspiration of infected secretions into the finer peripheral bronchi and alveoli gives rise to diffuse patchy infiltration of this type, distributed along the course of the bronchi of the involved pulmonary segment (Fig. 3).

The upper lobes were involved more frequently than in the more usual pneumonias: Right upper lobe, 5 times; right lower lobe, 6; left upper lobe, 3; left lower lobe, 4. In 4 instances there was an associated atelectasis. Except in these 4 patients, 2 of whom died, pneumonia did not appear to be a particularly serious complication. Presumably this was due to the routine administration of antibiotics to all patients with bulbar poliomyelitis.

Atelectasis: Atelectasis was the most common pulmonary complication met with in this study, occurring in 22 patients, of whom 13 were females and 9 were males. Atelectasis of one or more regions, accompanied by pneumonia and acute gastric dilatation, each in 2 instances, was present in all 7 patients who died.

A lesion was considered to represent atelectasis when it was definitely contractive or was accompanied by secondary signs of contraction such as narrowing of the rib cage, elevation of the corresponding diaphragm, ipsilateral shift of the mediastinum, etc. In general, atelectasis is produced by the complete obstruction of a bronchus supplying either an entire lung, lobe, or pulmonary segment. Obstruction

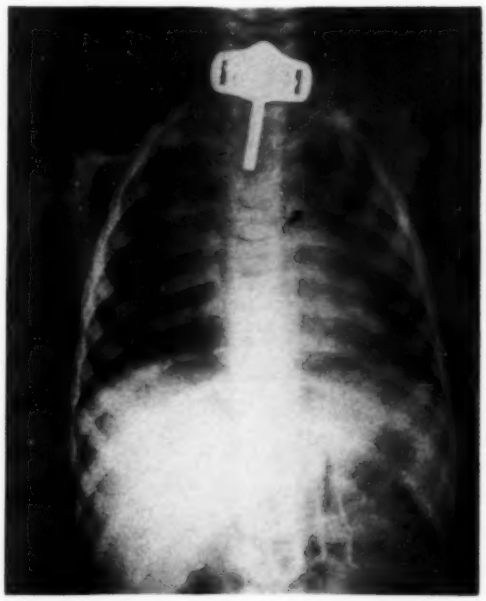


Fig. 3. Pneumonia and mediastinal emphysema. C. V. W., female, age 2 1/2 years, admitted Aug. 31, 1949, with acute bulbar spinal poliomyelitis, seven days after onset of symptoms. Thick speech and slight difficulty in swallowing. Diaphragm and intercostal muscles normal. Tracheotomy performed and patient placed in respirator Sept. 3. Moderate amount of secretions, becoming thick and purulent, Sept. 7. Temperature normal Sept. 5, rising to 101.2 Sept. 6. Patient transferred to secondary hospital Sept. 14.

Roentgenogram of Sept. 7, 1949. Diffuse, patchy pneumonic infiltration extending from both hili. Arrow points to a small amount of air in left mediastinum.

of a bronchus supplying less than a pulmonary segment leads to atelectasis only when there is interference with the interalveolar exchange of air, as seen in pulmonary edema or pneumonia (12, 16). All authors are in agreement that secretional obstruction is the cause of atelectasis in bulbar poliomyelitis. While this obstruction occasionally may be due to an actual mucous plug, it has been the experience of one of us (S. R. C.), and is well demonstrated by our autopsy findings, that it is more often caused by the accumulation of thick mucoid or purulent secretion. Mucosal edema also plays an important role in narrowing the bronchial lumen.

The atelectasis was segmental in 10 and lobar in 15 instances, with the following distribution: right upper lobe, 9; right

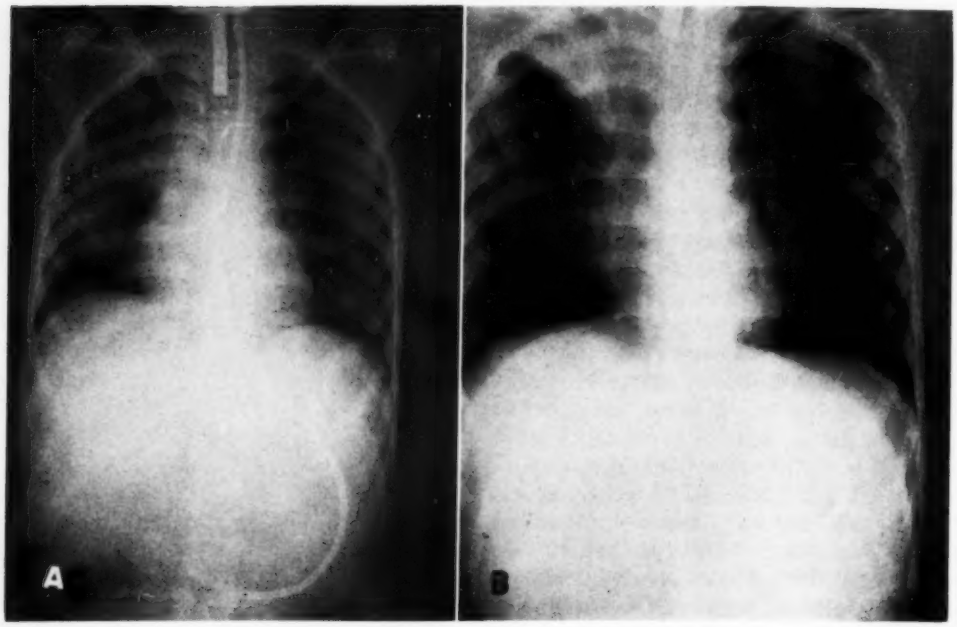


Fig. 4. Atelectasis with superimposed infection. I. M., female, age 12, admitted April 1, 1949, with acute bulbar spinal poliomyelitis, four days after onset of symptoms. Moderate weakness of diaphragm and intercostal muscles noted one day after admission. Inability to swallow. Large amount of nasal and pharyngeal secretions. Tracheotomy performed and patient placed in respirator April 2. Cyanotic episode April 17. Multiple bloody mucous plugs aspirated through tracheotomy tube April 18 and 19. Temperature 102° on admission; approximately normal by April 6; 101.6° on April 9, with rapid return to normal. Patient febrile from April 19 to 22, with temperature rising to 103.2°. White blood count 8,200 on admission, rising to 15,000 on April 11. Levine tube continuously in stomach. Patient transferred to secondary hospital April 27.

A. Roentgenogram of April 8, 1949. Contractive consolidation of the medio-basal segment of the right upper lobe. Levine tube in stomach. Minimal intestinal gas.

B. Roentgenogram of April 20, 1949. Atelectasis of right upper lobe. Note minimal intestinal gas accumulation in presence of gastric suction tube.

lower lobe, 7; left upper lobe, 2; left lower lobe, 4; entire right lung, 2; entire left lung, 1. As in the pneumonias, there was a comparative predominance of upper lobe lesions. Three patients had involvement of multiple lobes. Not all of these regions were atelectatic at the same time. Recurrent atelectasis of the same area was seen only once. Fourteen of the patients with atelectasis had evidence of superimposed infection as indicated by a significant rise in the temperature and usually the white blood count (Fig. 4). Minor areas of the atelectasis may have accompanied the pneumonic infiltrations but were too small to be recognized roentgenologically.

In view of the nature of the bronchial obstruction, it is not surprising that bronchoscopy was only occasionally successful. The obstruction was beyond the reach of the bronchoscope in most cases of segmental atelectasis. Spontaneous re-expansion was seen frequently in cases followed roentgenographically (Fig. 5).

Pulmonary Overexpansion: Atelectasis was frequently accompanied by mild overexpansion of the adjacent or opposite lung. In several instances the overexpansion was marked. In one patient with paralysis of the right diaphragm, atelectasis of the medio-basal segment of the right lower lobe, and scattered pneumonic infiltration throughout the remainder of the right lung, progressive overexpansion of the left lung developed, persisting after the right lung had cleared.

Bilateral pulmonary overexpansion without visible parenchymal disease occurred

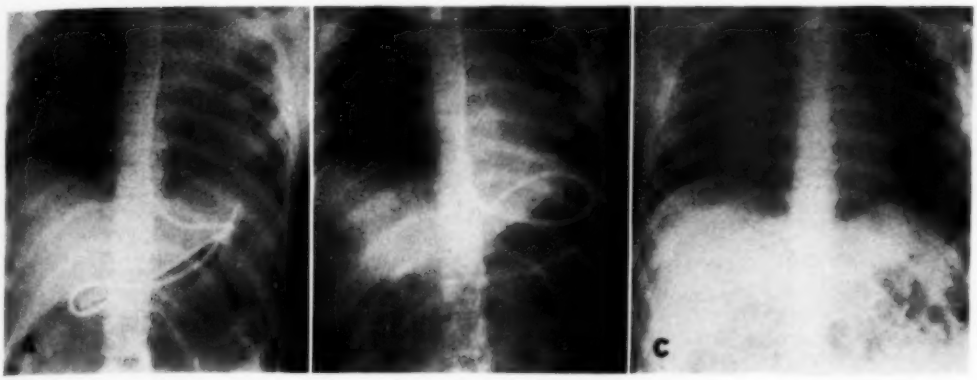
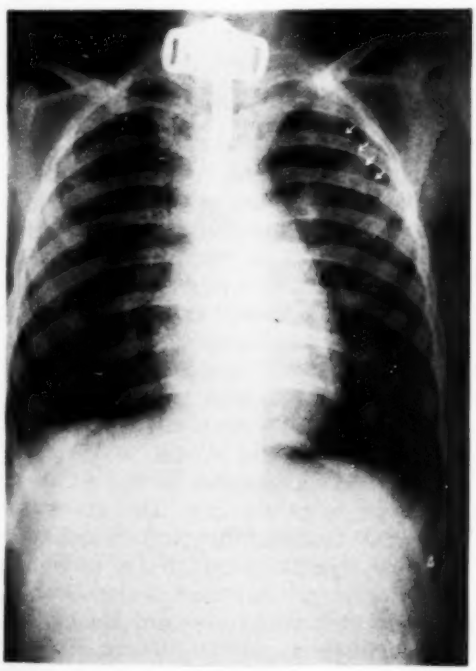


Fig. 5. Atelectasis with spontaneous re-expansion. P. D., female, age 17, five and a half months pregnant, admitted Sept. 20, 1949, with acute bulbar spinal poliomyelitis, five days after onset of symptoms. Slight dysphagia and weakness of diaphragm. Intercostal muscles normal. Placed in respirator on entry. Tracheotomy on following day. Moderate amount of thick secretion with many large plugs removed from tracheotomy tube. Cyanotic episode on Sept. 25. Bronchoscopy, Sept. 26, revealing a small amount of blood in right main bronchus and a large amount of blood and thick purulent mucus in the left main bronchus. Temperature 102° on admission, dropping rapidly to normal. Initial white blood count 9,700. No secondary rise of either white blood count or temperature. Normal delivery, Dec. 7, 1949. During transfer to secondary hospital, Dec. 18, generalized convulsions and acute gastric dilatation developed. Patient remained comatose and had intermittent convulsions until death, Feb. 20, 1950. Serious clinical consideration given to mechanical effect of acute gastric dilatation as cause of cerebral anoxia.

A. Roentgenogram of Sept. 27, 1949. Atelectasis of left upper lobe. Gastric suction tube. Moderate amount of intestinal gas.

B. Roentgenogram of Oct. 4, 1949. Spontaneous re-expansion of left upper lobe. Atelectasis of left lower lobe.

C. Roentgenogram of Oct. 31, 1949. Left lower lobe has re-expanded. Note absence of suction tube and moderate amount of intestinal gas.



in 2 patients, one of whom had an associated small left pneumothorax (Fig. 6). This patient, aged four, had a sudden episode of respiratory difficulty ten days prior to the taking of the roentgenogram, so that the exact sequence of events cannot be reconstructed. The other patient, aged five, experienced respiratory distress, with elevation of the temperature and white blood count, twenty days after admission to the hospital. The roentgenogram of the chest showed bilateral pulmonary over-

Fig. 6. Bilateral pulmonary overexpansion, pulmonary interstitial emphysema, and pneumothorax. B. A. A., female, age 4, admitted July 14, 1949, with acute bulbar spinal poliomyelitis, ten days after onset of symptoms. Diaphragmatic movement diminished. Intercostal muscles normal. Marked dysphagia. Moderate amount of secretion. Marked respiratory distress on July 16. Tracheotomy with immediate relief. Patient was not placed in a respirator. Temperature 100° on admission, rising to 101.2° and returning to normal by lysis. Patient lethargic on July 26, but no respiratory symptoms; temperature 102°. Transfer to secondary hospital Aug. 2.

Roentgenogram of July 26, 1949. Bilateral pulmonary overexpansion and small left pneumothorax. Arrows point to pleural margin. Pneumothorax may have occurred at time of respiratory distress on July 16.

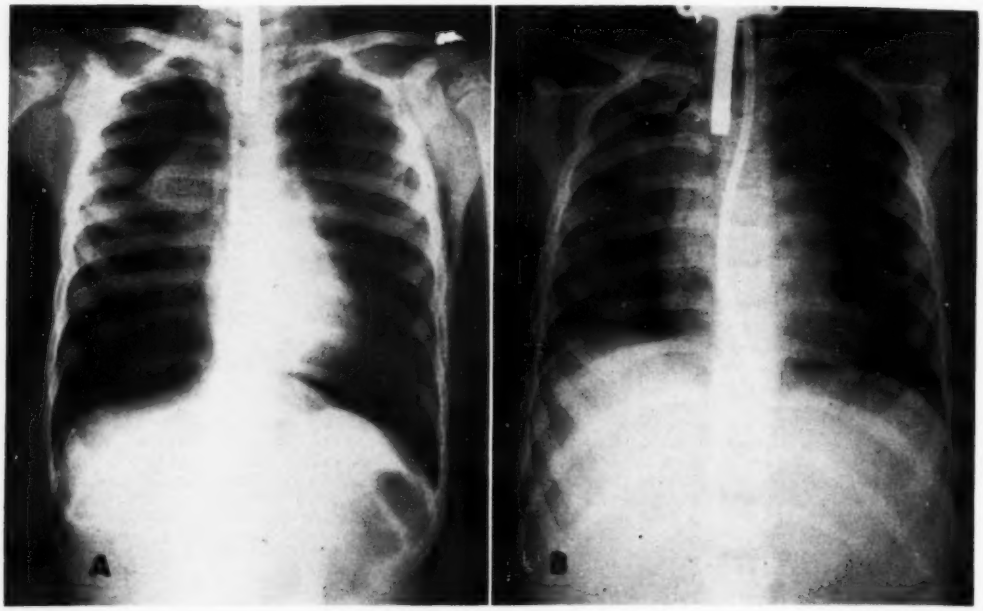


Fig. 7. Tension pneumothorax, mediastinal and subcutaneous emphysema, atelectasis, and pneumatocele. M. A. B., female, age 5, admitted Aug. 15, 1949, with acute bulbar spinal poliomyelitis, two days after onset of symptoms. Marked dysphagia. Diaphragmatic movement diminished. Intercostal muscles normal. Tracheotomy performed on admission because of cyanosis. Patient placed in respirator five hours later. Mediastinal and subcutaneous emphysema noted twelve hours after tracheotomy. Bronchoscopy on admission showed edema of the entire tracheobronchial tree and a small amount of thin secretion. All bronchial orifices were patent. Bilateral tension pneumothorax was relieved by continuous intercostal aspiration. Temperature, 102° on admission, returned to normal by lysis. Saliva greatly increased in amount. Levine tube in stomach continuously. Transfer to secondary hospital Sept. 1, 1949.

A. Roentgenogram of August 6, 1949. Bilateral tension pneumothorax, atelectasis of right upper lobe, mediastinal and subcutaneous emphysema.

B. Roentgenogram of August 10, 1949. Re-expansion of both lungs. Partial atelectasis of right upper lobe. Small pneumatocele indicated by arrow. Note gastric suction tube and absence of intestinal gas.

expansion with narrowing of the mediastinum. Both of these cases, it is believed, are examples of pulmonary interstitial emphysema as described by Macklin and Macklin (12). Lateral views of the chest might have demonstrated associated mediastinal emphysema (6, 12).

Pneumothorax and Mediastinal Emphysema: Four patients had pneumothorax, mediastinal emphysema, or both. Pneumothorax associated with bilateral pulmonary overexpansion was present in the case described above (Fig. 6).

Twelve hours after tracheotomy, mediastinal and extensive subcutaneous emphysema and a bilateral tension pneumothorax with almost complete collapse of both lungs developed in a five-year-old girl (Fig. 7). In addition, the right upper lobe was atelectatic. Following aspiration of the air from the pleural cavities, both lungs re-expanded rapidly. A small pneumatocele was then visible in the atelectatic right upper lobe. The relationships of respiratory tract disease and tracheotomy to the production of interstitial pulmonary emphysema, pneumothorax, and mediastinal and subcutaneous emphysema have been described in the classic monograph of Macklin and Macklin. Rupture of the pulmonary alveolar bases with escape of air into the interstitial tissues of the lung may follow atelectasis and hyperinflation of the adjoining or opposite lung. The air then passes along the vascular structures into the mediastinum and may follow the fascial planes into the subcutaneous tissues of the neck or

may rupture into the pleural cavity, producing a pneumothorax. While these changes may occasionally result from tracheotomy, this is most unusual. In most instances these lesions are either unrecognized at the time of tracheotomy or follow when tracheotomy fails to relieve the obstructed airway. Recently, Evans and Smalldon (6) have published an excellent review and discussion of the subject.

Pneumonia, accompanied by minute localized zones of emphysema and unrecognized small areas of atelectasis, may be associated with interstitial and mediastinal emphysema. Figure 3 illustrates the case of a girl of two and a half years with bilateral diffuse pneumonia who had minimal mediastinal emphysema as shown by the presence of air along the left cardiac border. Apparently insufficient air escaped to cause either subcutaneous emphysema or pneumothorax.

Following circulatory collapse and multiple episodes of respiratory distress, an encapsulated pneumothorax developed in a man of forty-four, at the base of the right thorax. Macklin and Macklin have pointed out that the pressure of interstitial air bubbles can reduce the flow of blood in the pulmonary vessels and cause circulatory collapse. It may be that some of the cases of circulatory failure in bulbar poliomyelitis are caused by pulmonary interstitial emphysema rather than by acidosis, anoxia, or viral infection of the circulatory center of the brain.

Pulmonary Edema: Pulmonary edema was not recognized either clinically or roentgenologically in any of our cases, though it has been mentioned repeatedly as being a serious complication of bulbar poliomyelitis (2, 5, 7, 13). One of the patients was found to have pulmonary edema at autopsy, apparently developing terminally.

Elam (5) believes that pulmonary edema is due to a lack of oxygen in the alveolar air and obstruction of the airway. He found that the maintenance of positive pressure during the inspiratory phase of respiration and a high concentration of oxygen were most helpful in its prevention. Perhaps the absence of clinically recognizable pulmonary edema in our cases was due to the fact that almost all of the patients received inspiratory positive pressure and oxygen therapy.

Pneumatocele: Obstructive emphysema with pneumatocele formation was observed in 2 patients. In one case it occurred in a segmental atelectasis with superimposed infection of the right upper lobe. In the other it was seen in a re-expanding atelectatic right upper lobe following bilateral pneumothorax and mediastinal and subcutaneous emphysema (Fig. 7).

Pleural Fluid: Minor amounts of pleural exudate were occasionally seen adjacent to the inflammatory lesions. In one patient a moderate amount of fluid was present in association with a localized pneumothorax. Aspiration was not necessary.

* * * * * *

Many of the problems discussed here remain unanswered. Their solution depends on further correlation of clinical, roentgenological, and pathological findings. Such studies are in progress. More adequate roentgenographic facilities than are now available must be developed. Both the x-ray apparatus and respirator should be designed so as to permit easy, rapid examination, preferably without removing the patient from the respirator. More frequent examinations would be possible than are obtainable at present. Every patient with bulbar poliomyelitis, if practicable, should have a roentgen examination of the chest on admission to the hospital and before having a tracheotomy or being placed in a respirator. In those patients in the respirator or with a tracheotomy, the examination should be repeated at routine intervals; more frequent examinations are indicated when a pulmonary complication is suspected or has been demonstrated.

SUMMARY

A representative group of 53 patients with acute bulbar poliomyelitis admitted

to the Los Angeles County Hospital in 1949 was analyzed as to roentgenologically demonstrated pulmonary complications and various clinical features which may have influenced their development.

Thirty-one (58 per cent) of the patients had pulmonary complications. The following lesions were observed: pneumonia, atelectasis, pneumatocele, pulmonary overexpansion, pulmonary interstitial emphysema, mediastinal emphysema, and pneumothorax. The incidence and pathogenesis of these lesions are discussed.

Atelectasis was the most common lesion, occurring in 22 patients, 7 of whom died. Two of these patients had associated pneumonia. None of the other pulmonary complications were noted in those who died.

While pulmonary complications occurred in 20 females as compared to 11 males, 6 of the 7 patients who died were males. Pulmonary complications developed more frequently in patients below six years of age.

An increased amount of intestinal gas was noted in most patients. Gastric distention was particularly common. Acute gastric dilatation occurred in 4 patients, 3 of whom had associated pulmonary lesions. Two of these 3 patients died. Intestinal gas was effectively controlled by continuous gastric suction.

The incidence of pulmonary complications was highest in those patients who had the largest amount of nasal, pharyngeal, and tracheobronchial secretions.

There was no correlation between pulmonary complications and the time of tracheotomy or entry into the respirator after admission, but the time relationship of these latter factors to each other was significant. In 13 out of 17 patients who had tracheotomies one day or more *after* they were placed in a respirator pulmonary complications developed. Six of the 7 deaths occurred in this group. No increase in incidence was noted in those who had tracheotomies *before or at the time* of being placed in a respirator.

Analysis of such clinical features as duration of symptoms before admission to the hospital, difficulty in swallowing, paralysis of the diaphragm and intercostal muscles, temperature, and initial white blood count yielded no clues as to which patients might show pulmonary complications.

NOTE: We are grateful to Drs. Albert G. Bower and Evelynne G. Knouf, of the Department of Communicable Diseases, and Drs. J. MacKenzie Brown and Alden H. Miller of the Department of Otolaryngology, for their helpful suggestions and criticisms in the preparation of this paper.

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SUMARIO

Complicaciones Pulmonares de la Poliomielitis Bulbar Aguda

Un típico grupo de 53 enfermos con poliomielitis bulbar aguda fué analizado con respecto a la presencia de complicaciones pulmonares observables roentgenológicamente y de varias características clínicas que pueden haber afectado la aparición de las primeras.

Treinta y un enfermos (58 por ciento) tenían complicaciones pulmonares, habiéndose observado las siguientes lesiones: neumonía, atelectasia, neumatocele, hiperexpansión pulmonar, enfisema intersticial pulmonar, enfisema mediastínico y neumotórax. La atelectasia fué la lesión más frecuente, existiendo en 22 pacientes, 7 de los cuales fallecieron. Dos de éstos tuvieron neumonía concomitante. En los fallecidos, no se notó ninguna de las otras complicaciones pulmonares.

Aunque hubo complicaciones pulmonares en 20 mujeres, comparado con 11 varones, 6 de los 7 fallecidos fueron varones. Las complicaciones pulmonares aparecieron más frecuentemente en enfermos de menos de seis años de edad.

En la mayor parte de los sujetos notóse aumento de la cantidad de gases presentes en el intestino. La distensión gástrica fué en particular común. En 4 enfermos hubo dilatación aguda del estómago, teniendo 3 de ellos además lesiones pulmonares. Dos de estos 3 fallecieron. El meteorismo intestinal fué cohibido en forma eficaz por la continua succión gástrica.

La incidencia de complicaciones pulmonares alcanzó su máximo en los sujetos que tenían la proporción mayor de secreciones nasales, faríngeas y tráqueobronquiales.

No hubo correlación entre las complicaciones pulmonares y el tiempo de la traqueotomía o de la entrada en el respirador después del ingreso, pero revistió importancia la mutua relación cronológica entre los últimos factores. En 13 de 17 enfermos traqueotomizados un día o más después de ser colocados en un respirador, se presentaron complicaciones pulmonares. Seis de las 7 muertes correspondieron a ese grupo. No se notó aumento de la incidencia en los traqueotomizados antes, o en el momento, de ser colocados en el respirador.

El análisis de las características clínicas, tales como la duración de los síntomas antes del ingreso en el hospital, disfagia, parálisis del diafragma y de los músculos intercostales, temperatura y leucocitosis inicial, no aportó claves indicativas de qué enfermos revelarían complicaciones pulmonares.

Reticulo-Endotheliosis

(Hand-Schüller-Christian Disease)[1]

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THERE IS considerable confusion of terminology regarding the group of diseases known as "Hand-Schüller-Christian disease," "Letterer-Siwe disease," and "eosinophilic granuloma of bone." This confusion might be expected as a result of varying concepts of their pathogenesis. The relationship of lipoid to the conditions, which was emphasized by Rowland (1) has been reflected in the widespread use of terms designating the presence of lipoid material in the lesions. Since reticulo-endothelial cells also are present, modifications of the terminology to indicate their presence have been proposed. To the words "lipoid" and "reticulo-endothelial," a third term has been added in an effort to describe another variant of the disease, namely, "granuloma," indicating chronicity and a tendency to healing with fibrous tissue and collagenization. All possible combinations of these terms may be found in the medical literature, depending on the particular phase of the disease that is prominent in the case or cases reported. None of the designations that have been proposed is entirely satisfactory and we have no new one to suggest. Because of the apparent basic relationship of Hand-Schüller-Christian disease, Letterer-Siwe disease, and eosinophilic granuloma, it would seem that a fairly general term which would be descriptive, inclusive, and yet fairly specific is to be desired. Until this can be found, we shall refer to these diseases as the reticulo-endothelial group and specify the type, as Hand-Schüller-Cnristian disease, Letterer-Siwe disease, or eosinophilic granuloma, if possible. It may be that "systemic reticulo-endothelial granulomatosis," as suggested by Wallgren (2) is the best designation for the group, although it does have certain features that make it not entirely satisfactory.

Concepts of the pathogenesis of this group of diseases have changed through the years. As more of the aspects of the condition have become evident, emphasis has been placed on different phases. The syndrome of diabetes insipidus, exophthalmos, and defects of the membranous bones was originally described by Hand (3) in 1893 as a tuberculous granuloma of bone with some secondary hypophyseal involvement. In 1915 Schüller (4) reported 2 cases with defects in the membranous bones of the skull, and in 1920 Christian (5) also reported a case with lesions of the skull, but he felt that the disease was related to some pituitary dysfunction.

In 1928 Rowland postulated that the lesions in this group of diseases were due to excessive amounts of lipoid in the body fluids. This excess, he believed, caused irritation of the vessel walls and perivascular infiltrations, the latter increasing progressively in size because of "blockage of the reticulo-endothelial system." Thannhauser and Magendantz (6) later stated that there was no definite proof of the assumption that primary essential xanthomatosis was caused by a disorder of cholesterol metabolism. In their opinion the metabolic disturbance, if there is one, is localized in those cells which are already xanthoma cells because they contain fat. The primary lesion is then a proliferation of reticulo-endothelial cells associated with some intracellular metabolic disturbance, causing them to store certain forms of fat.

Rowland has stated that the histologic manifestations of Hand-Schüller-Christian

[1] From the Section on Roentgenology and the Section on Pediatrics, Mayo Clinic, Rochester, Minn. Presented at the Thirty-sixth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 10–15, 1950.

disease are variable. Early in the disease the lesions are made up of foam cells, later almost entirely of spindle cells and connective tissue; in older lesions there are frequently no lipoid-containing cells.

In Wallgren's opinion the early histologic findings of Hand-Schüller-Christian disease are those of non-lipid reticuloendotheliosis, followed by the appearance of foam cells with fat and eventually fibrous or scar tissue without any fat. Foam cells may develop in older lesions but those of recent origin are reticulum-cell proliferations. It was Wallgren's belief that the accumulation of cholesterol was not an essential feature of the disease.

Gross and Jacox (7) reviewed 84 reported cases of Hand-Schüller-Christian disease and found that in 26 cases the presence or absence of foam cells was not even mentioned. In 9 cases necropsy and biopsy material showed no foam cells. Eosinophilic infiltration was noted in 29 of the 84 cases.

Sosman (8) suggested that foam cells were not always present. Chester and Kugel (9) and Lane and Smith (10) expressed the belief that they were present in the early stages of the disease and disappeared during the healing phase. Green and Farber (11) described the appearance of foam cells associated with a late stage of the disease. Letterer (12) stated that cholesterol infiltration represented merely an associated feature.

The difference in opinion among the authors cited above suggests that the histologic appearance may be quite variable, and this has been true in our experience. Foam cells are present in some cases and not in others. Giant cells are commonly observed. In tissues from most of the patients there is a moderate number of leukocytes. Eosinophilia varies in degree. In some specimens of tissue, necrosis has been a prominent feature. Occasionally some fibrosis and collagenization have been noted.

In 1924 Letterer reported the first case of the disease that was later to bear his name, and in 1933 Siwe (13) collected the available cases and grouped them together. In 1936 Abt and Denenholz (14) reported a case and proposed the name "Letterer-Siwe's disease" to describe the syndrome characterized by splenomegaly, hepatomegaly, hemorrhagic tendency, generalized lymphadenopathy, localized tumors over bones, secondary anemia, increase in non-lipoid-containing macrophages, and relatively short duration with fatal outcome.

The histologic characteristics of Letterer-Siwe disease are based on the presence of non-lipoid storing reticulum cells relatively large in size and round or polygonal in shape. The cytoplasm is pale-staining and the nucleus is chromatic. There are occasional multinucleated giant cells and some increase in the reticular fibers. Wallgren expressed the belief that so-called infectious reticulo-endotheliosis and Letterer-Siwe disease are identical, and that any infection is incidental rather than causative.

Wallgren has suggested further that the only essential difference between Letterer-Siwe disease and Hand-Schüller-Christian disease is a storage of cholesterol in foam cells in the latter. He also stated that foam cells occur only in those cases of that disease in which the duration has been three months or more, and that they are always found if the disease has been present more than twelve months. The lack of foam cells in Letterer-Siwe disease may be explained by its rapid termination, which prevents their accumulation. Their presence or absence, however, cannot be used as a differential point in the diagnosis of Hand-Schüller-Christian disease.

There are certain clinical differences between Letterer-Siwe disease and Hand-Schüller-Christian disease. The classic triad of diabetes insipidus, exophthalmos, and defects in the calvarium does not occur in Letterer-Siwe disease. In Hand-Schüller-Christian disease the bone lesions are predominantly in the calvarium. When bone lesions occur in Letterer-Siwe disease, they are more likely to involve many bones, though occasionally they are limited to the skull.

Jaffe and Lichtenstein (15) and Otani

and Ehrlich (16) independently reported cases of eosinophilic granuloma of bone. This disease is characterized by local tenderness and pain with local swelling. The lesions are sometimes solitary but may be multiple. Histologically they present sheet-like collections of histiocytes, an accumulation of eosinophilic leukocytes, hemorrhage, necrosis, and multinuclear giant cells showing some phagocytic activity.

Gross and Jacox have considered eosinophilic granuloma of bone and Hand-Schüller-Christian disease as manifestations of the same basic malady. The histologic features are very similar, consisting of granulomatous tissue in which reticulo-endothelial cells predominate and in which eosinophils are usually found. The eosinophilia of the peripheral blood and the hypercholesteremia are too inconsistent to be of much value as common characteristics of the two diseases.

Farber (17) has suggested that clinically the cases of eosinophilic granuloma should be singled out but that anatomically and histologically the disease is related to Hand-Schüller-Christian disease and Letterer-Siwe disease.

Mallory (18) has classified this group of diseases according to the most frequent age of incidence. Letterer-Siwe disease occurs in infancy or early childhood. It is often rapidly fatal and the lesions are usually widely distributed through the soft tissues. Occasionally the bones are involved. Hand-Schüller-Christian disease occurs in children or adults in chronic form; the skeletal lesions frequently heal and there is somewhat less involvement of the viscera than in Letterer-Siwe disease. Healing occurs by replacement of reticulo-endothelial cells with fibrous tissue and cholesterol deposits. Eosinophilic granuloma of bone in children and young adults involves the bone primarily, with little or no involvement of viscera. It is a comparatively benign and localized form of the disease in which the bone lesions may be multiple or solitary and in which the outcome is usually favorable.

A careful study of the cases of reticuloendotheliosis that have been reported and an analysis of data on the cases encountered at the Mayo Clinic reveal several examples which can be interpreted only as transitional forms of the disorder. A single case may present some of the characteristics of eosinophilic granuloma of bone or of Hand-Schüller-Christian disease or of Letterer-Siwe disease. Often it is not possible to classify the case definitely as any one of these three conditions. Hertzog, Anderson, and Beebe (19) reported a case which was interpreted as a transitional form between Hand-Schüller-Christian disease and malignant lymphoblastoma of the reticuloendothelial type.

In 21 of our 28 cases biopsy was performed. Of these, 16 were considered to be Hand-Schüller-Christian disease or xanthomatosis and 5 were thought to be examples of eosinophilic granuloma. Clinically there were 3 cases of Letterer-Siwe disease included in the 16 cases of Hand-Schüller-Christian disease. Probably one reason for the confusion in this group of diseases is the difficulty confronting the pathologist who is required to categorize these diseases from a bit of tissue which may represent any phase of any one of them or even a transitional form with characteristics of any or all of the group.

CLINICAL ASPECTS

As has been pointed out, originally the term "Hand-Schüller-Christian disease" designated the syndrome characterized by exophthalmos, diabetes insipidus, and granulomatous lesions of the skull. Many cases have since been reported with parts of the classic triad missing or with other signs or symptoms, including lymphadenopathy, skin lesions, splenomegaly, hepatomegaly, pulmonary involvement, anemia, and disorders of the blood.

The clinical signs and symptoms in our 28 cases, and their incidence, are recorded in Table I. In 10 of the 28 cases none of the signs or symptoms listed was present.

Reticulo-endotheliosis is not usually associated with other diseases, though Grady

TABLE I: INCIDENCE OF SIGNS AND SYMPTOMS OF RETICULO-ENDOTHELIOSIS IN 28 CASES

Sign or Symptom	Cases
Exophthalmos	8
Lymphadenopathy	9
Hepatomegaly	7
Splenomegaly	5
Polyuria	6
Skin lesions	4
Pulmonary manifestations	4

and Stewart (20) reported a case of Hand-Schüller-Christian disease in which tuberculosis was present. In none of the cases seen at the Mayo Clinic was any concomitant disease observed.

The lesions of the skull in reticulo-endotheliosis present a firm, non-tender swelling in the scalp over the area involved.

Eosinophilic granulomas occur more frequently in young adults than in patients of other ages. Pain is usually the presenting symptom. Often there is tender swelling of the soft tissue adjacent to the bone lesion. Fever, anorexia, loss of weight, and malaise may be present. As in Hand-Schüller-Christian disease, males tend to be predominantly affected. Dundon, Williams, and Laipply (21) found that in 64 per cent of the cases reported up to 1945 the patients were less than twenty years of age. Leukocytosis and eosinophilia are not uncommon.

Lymphadenopathy has not been considered to be a primary sign of Hand-Schüller-Christian disease and yet it occurs in this syndrome as well as in Letterer-Siwe disease. Freund and Ripps (22) reported a case, with onset at seven weeks of age, in which the primary manifestation was lymph node enlargement. At thirteen months granulomatous defects appeared in the bones. Flori and Parenti, cited by Jaffe and Lichtenstein, reported a case with enlargement of lymph nodes in which, at necropsy, the typical granulomas of Hand-Schüller-Christian disease were found. We have also had a case in which the preliminary diagnosis of Hodgkin's disease was made because of enlarged lymph nodes, only to find subsequently some of the roentgenologic and pathologic manifestations of Hand-Schüller-Christian disease.

Chester and Kugel stated that 50 per cent of cases of Hand-Schüller-Christian disease have occurred in children less than five years of age, and that males outnumber females two to one.

Dauksys (23) reviewed 124 cases of xanthomatosis and reported that more than half the patients were less than six years of age and that two thirds were less than twelve years of age.

In the 28 cases reviewed by us the average age of onset of the disease was about 3.5 years. The latest onset was at thirteen years and more than 50 per cent of the cases began before the age of two (Table II).

TABLE II: AGE AT ONSET IN 28 CASES OF RETICULO-ENDOTHELIOSIS

Age	Cases
6 to 12 months	5
12 to 18 months	4
18 to 24 months	6
24 to 30 months	3
30 to 36 months	2
36 months to 48 months	4
5 years	1
8 years	1
13 years	2

Although reticulo-endothelial granulomatosis is primarily a disease of children, older persons may be affected. Currens and Popp (24) reported a case of xanthomatosis in a woman aged twenty-nine years, with lesions in the skull and femur and extensive involvement of the lungs. Versiani, Figueiro, and Junqueira (25) presented the case of a woman of fifty with lesions in the left femur which on biopsy showed granulomatous tissue with foam cells and eosinophils.

It was found in our 28 cases that the disease was twice as common in males as in females.

ROENTGENOLOGIC ASPECTS

The roentgenologic manifestations of reticulo-endothelial granuloma in the skeleton consist of areas of destruction, multiple or solitary, and involving one or more bones. The bones most frequently affected are those of the skull. Of the 28 cases reviewed, only 3 failed to show some evidence of involvement of the skull. The

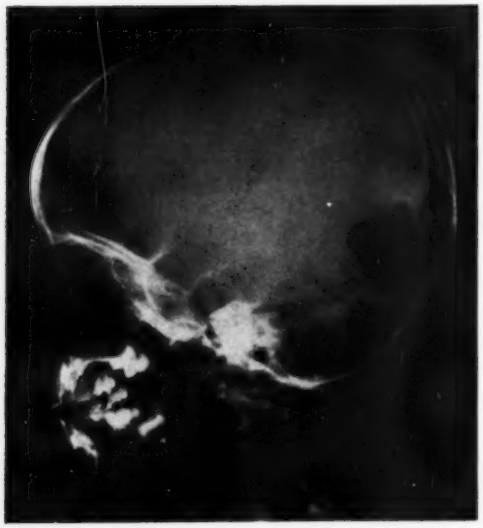


Fig. 1. Large area of destruction in the skull of a child aged two years. Many other bones involved. Biopsy reported as indicating eosinophilic granuloma.

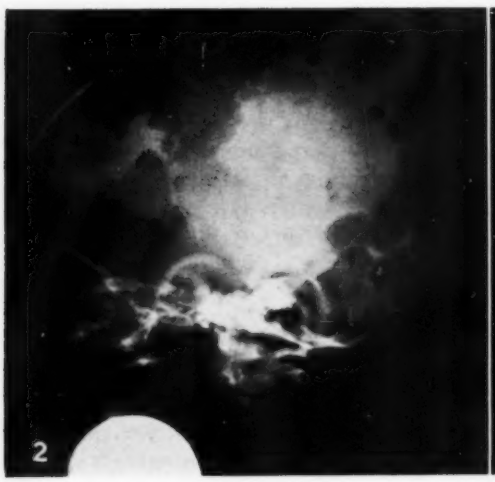
frequency with which other bones are affected is shown in Table III. As can be seen from the table, the pelvis, femur, ribs, humerus, and scapula are the more common sites after the skull. Involvement below the elbow and knee is unusual and vertebral lesions are also rare.

TABLE III: FREQUENCY OF INVOLVEMENT OF BONES OTHER THAN THOSE OF THE SKULL IN 28 CASES OF RETICULO-ENDOTHELIOSIS

Site	Cases
Pelvis	13
Femur	11
Rib	10
Humerus	10
Mandible	9
Scapula	7
Tibia	6
Radius	4
Ulna	3
Clavicle	3
Vertebrae	3
Fibula	2
Calcaneus	1
Phalanx	1
Hip	1

Of the 28 cases, 5 showed single lesions, located in 4 instances in the skull. In 1 case there was a solitary lesion in the pelvis and in 1 case no bone lesions were found.

The areas of destruction shown in roentgenograms of the skull are fairly sharply demarcated, with irregularly scalloped margins (Fig. 1) shading off into normal bone. Rarely is either the inner or the outer table of the skull intact. As the lesion grows, it destroys the bone along its margins, leaving no normal bone in the center of the area of destruction. The skull lesions do not show any margin of



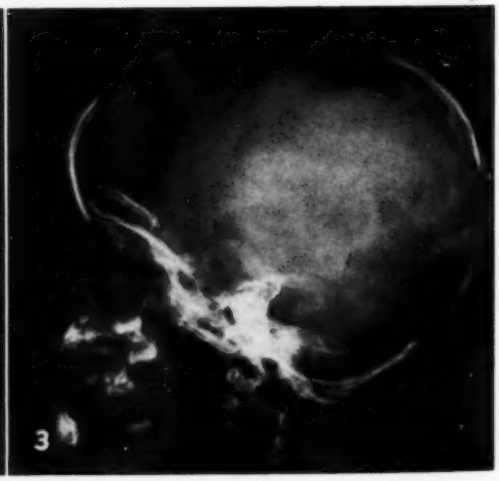


Fig. 2. Skull lesions in a boy aged three and a half years, whose treatment had to be stopped because of leukopenia. Late stage of the disease with extensive destruction. Involvement of many other bones. Biopsy reported as eosinophilic granuloma.

Fig. 3. Multiple defects in the calvarium in a girl of three years. Involvement of other bones. Biopsy reported as eosinophilic granuloma.

reaction until after treatment. Since the skull is affected more frequently and earlier in the course than other regions, the lesions may be quite large before discovery or, if treatment is ineffectual, tremendous defects may occur as the disease progresses (Fig. 2). There seems to be no relationship between the size of the lesions and any other factor in the disease. The larger lesions are usually solitary, but they may be associated with smaller lesions (Fig. 3). Periosteal reaction is lacking in the skull.

The lesions occurring in the pelvis and scapula are very similar in appearance to those in the skull (Fig. 4).

The variation in form of the disease appears to take place chiefly in the long bones. When reticulo-endotheliosis occurs in the shaft of a long bone, it may or may not produce expansion of the shaft, and this cannot be used as a point of differentiation between Hand-Schüller-Christian disease and eosinophilic granuloma, as suggested by Bass (26). Irregular destruction of the bone may sometimes produce a trabeculated appearance (Fig. 5). The lesions may occur anywhere in the shaft but they tend to be present more commonly in the distal or proximal segments than elsewhere. The epiphysis is usually spared, though we have seen one case in which there was questionable involvement of the epiphysis either by contiguous spread or by the development of a separate lesion (Fig. 6). As the lesions increase in size, they destroy the inner surface of the cortex, and pathologic fractures often occur.

Usually there is no zone of reaction or marginal sclerosis around the radiolucent area in the bone until after treatment is begun. Periosteal reaction is not uncommon and varies greatly in degree. In some cases, particularly those which have been designated eosinophilic granuloma, there may be considerable reaction in the adjacent bone with lamellation (Fig. 7). The amount of reaction at the site of the lesion does not seem to have any relationship to the development of multiple lesions (Fig. 8).

Roentgenograms of the thorax in those patients with pulmonary involvement reveal a rather fine nodular density scattered throughout the lungs along the distribution of the bronchovascular markings (Fig. 9). Chester and Kugel reported a case in which at necropsy the pulmonary lesions were found to be small, irregular nodules, varying in diameter from 0.5 to 2.0 cm. Currens and Popp reported a case of Hand-Schüller-Christian disease, in a woman aged 29 years, with a diffuse granulomatous infiltration of the lungs. Treatment was given to only one side of the thorax and the treated side showed some improvement. When healing takes place, the lesions may either disappear or be seen as irregular linear strands of fibrosis, depending on the extent of involvement. In patients with severe pulmonary involvement with healing, the fibrosis seems to be

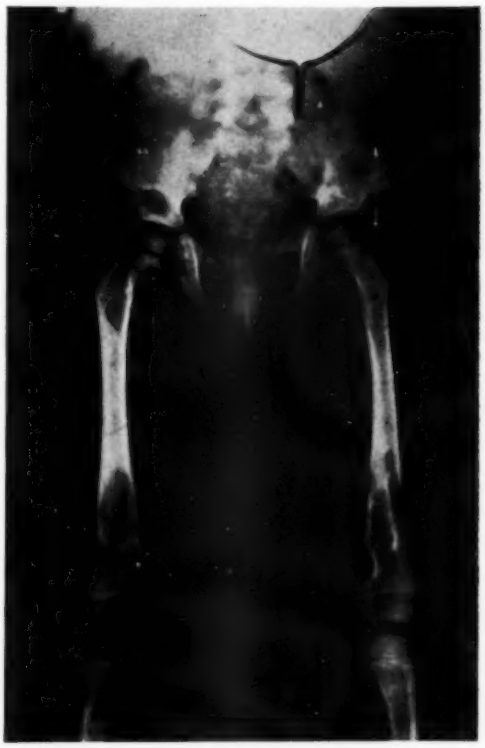
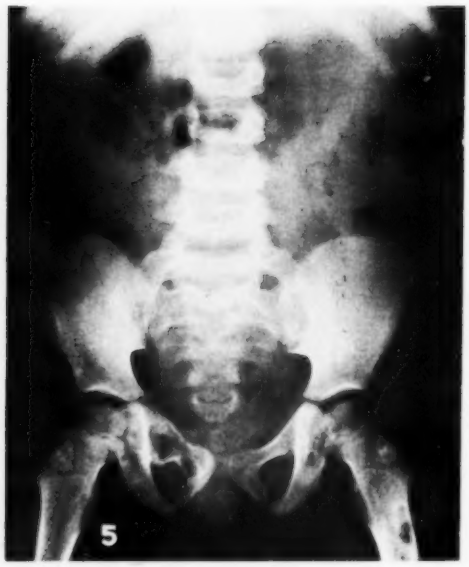
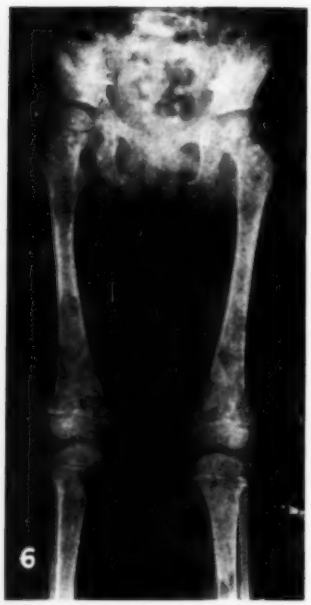
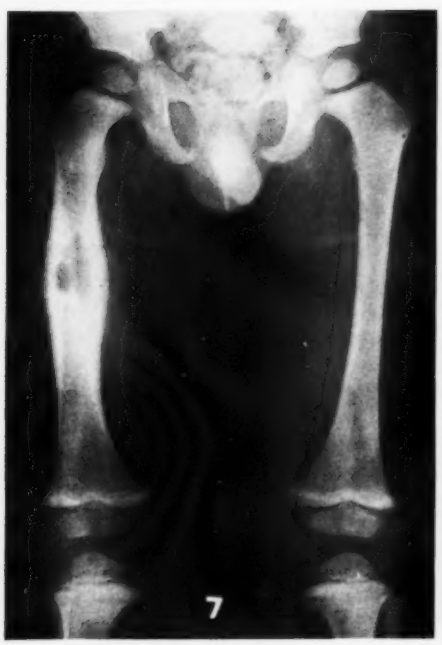


Fig. 4. Lesions in pelvic bones and femora in a boy of twenty-one months. Possible epiphyseal involvement of lower portion of left femur. Patient living and well twenty-three years later.







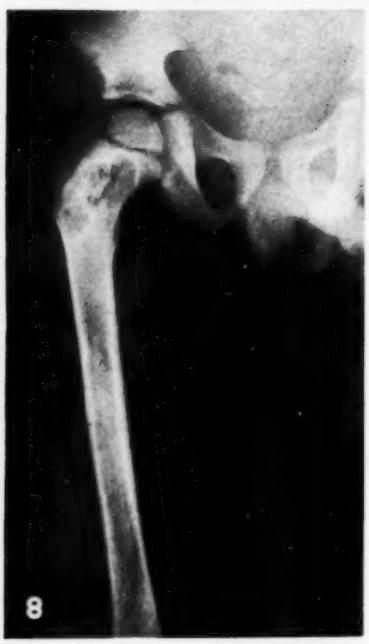


Fig. 5. Lesion in right ischium and pubis, presenting some appearance of trabeculation, in a girl of four years. There is also a lesion in the left femur. Biopsy reported as compatible with xanthomatosis.

Fig. 6. Multiple lesions of the pelvis and lower extremities in a boy aged three years. Involvement of tibial epiphysis.

Fig. 7. Area of destruction with considerable reaction and periosteal proliferation in a boy of twenty-eight months. Biopsy reported as eosinophilic granuloma.

Fig. 8. Same case as Fig. 7, six months later. The old lesion has healed but a new lesion has developed in the neck of the femur. Many other bones, including the skull, were involved.

more prominent in the lower than in the upper portions of the lung fields.

When the disease involves the mandible, there is destruction of bone around the roots of the teeth. In the roentgenogram teeth surrounded by this granulomatous process appear to be floating in the mouth (Fig. 10). Chester and Kugel reported a case in which almost all of the teeth had fallen out by the time the patient had

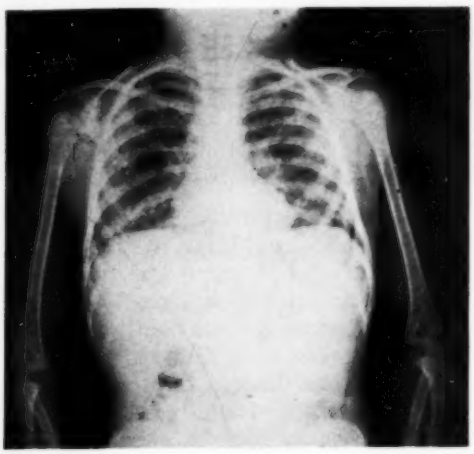


Fig. 9. Extensive small nodular lesions scattered throughout the lung fields in a girl of two and a half years. Biopsy reported as compatible with Hand-Schüller-Christian disease.

reached twenty-three years of age. Hamilton, Barner, Kennedy, and McCort (27) reported a case of eosinophilic granuloma with loosening of the teeth, although there were no proved visceral manifestations of the disease. The teeth may fall out or may be lifted out, and both the deciduous and the permanent teeth may be affected. There is no other disease which affects the mandible and the teeth in quite this fashion, and when the picture is encountered one must be strongly suspicious of reticulo-endotheliosis.

The roentgenographic changes in eosinophilic granuloma and Letterer-Siwe disease are indistinguishable from those of Hand-Schüller-Christian disease. A solitary lesion in a long bone in a young male with periosteal reaction would be suggestive evidence of eosinophilic granuloma.

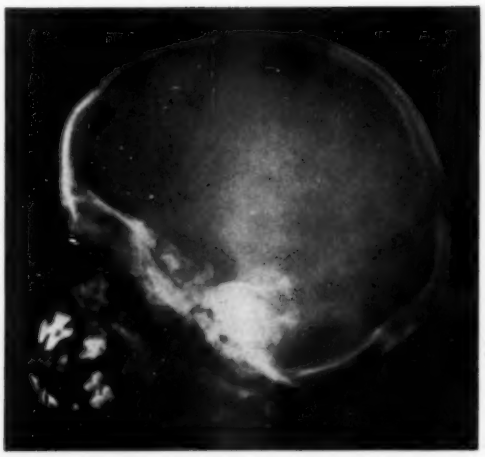


Fig. 10. Multiple defects in the skull in a girl aged four years; involvement of the mandible, with "floating teeth."

An area of destruction in bone in an infant is more characteristic of Letterer-Siwe disease, but the roentgenographic appearance alone would not be conclusive.

DIFFERENTIAL DIAGNOSIS

Among other diseases in which areas of bone destruction are encountered in the skeleton are those with systemic involvement, such as metastatic carcinoma and multiple myeloma, and localized lesions of the skeleton—particularly the skull—such as meningiomas, epidermoid cysts, and osteomyelitis. Metastasis and myeloma may be indistinguishable roentgenologically from reticulo-endotheliosis (Fig. 11). Myeloma fortunately is rare in children (Fig. 12). Differential diagnosis may have to be made by clinical means, by some laboratory method, or by biopsy. In general, tumors of the skull do not present the type of destruction seen in reticulo-endotheliosis. In osteomyelitis the destructive process may leave areas of uninvolved bone in the center of the lesion, or there may be production of bone associated with destruction, neither of which is characteristic of the lesions of reticulo-endotheliosis.

When the disease occurs in the long bones, it is frequently more difficult to be certain of the diagnosis by roentgenologic

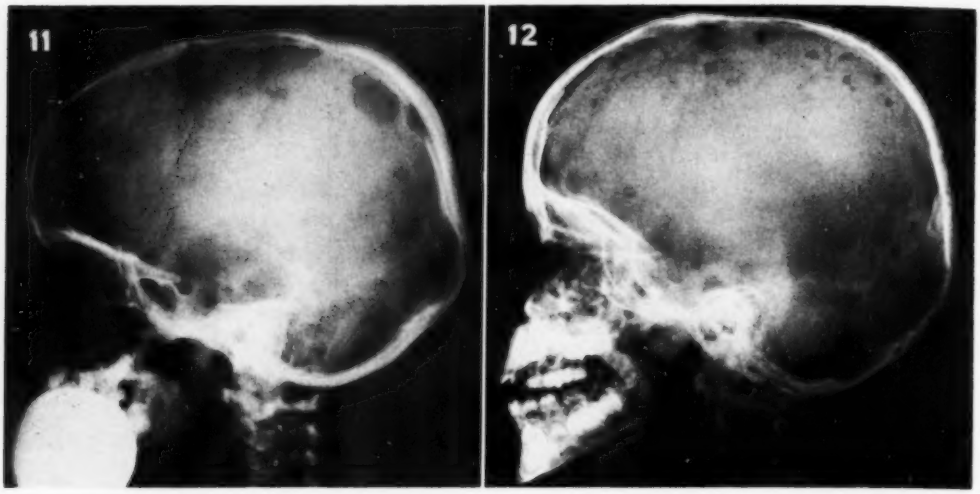


Fig. 11. Multiple defects of the skull in a boy of nine years, due to a metastatic malignant lesion, Grade 4. Origin undetermined.
Fig. 12. Multiple small areas of destruction in the calvarium due to multiple myeloma in a boy of five years.

methods only than when it occurs in the skull. Eosinophilic granuloma may resemble Ewing's sarcoma closely, particularly if the lesion is solitary. Ahlström and Welin (28) reported a case in which the roentgenologic differentiation between these conditions was very difficult. Myeloma, a metastatic tumor, osteomyelitis. chondromas, giant-cell tumors, and occasionally fibrous dysplasia occurring in long bones may resemble reticulo-endotheliosis.

In our experience pulmonary findings have never occurred without some associated lesions in the skeleton, with a single exception, in which the lungs were involved primarily and a defect in the calvarium appeared later. As a general rule there is no pulmonary involvement unless skeletal lesions are also present, and usually the skeletal involvement is extensive.

Reticulo-endotheliosis should be suspected in any child in whom there is an irregular defect in the skull.

COURSE AND PROGNOSIS

The average duration of active disease in the cases of reticulo-endotheliosis seen at the Mayo Clinic was slightly more than two years. The longest duration of active disease was six years. Characteristically, while one lesion is healing, another may be developing at some other point in the skeleton, either close to or distant from the site of the original defect. Kalbitzer (29) reported a case of Hand-Schüller-Christian disease with periodic observations from five weeks up to eight years of age, when the lesions finally disappeared.

New lesions may develop quite rapidly, over a period of from two to six weeks, to become recognizable roentgenologically. In the case records of the Massachusetts General Hospital (30) there is a report of a girl aged seventeen years in whom a defect in the skull measuring 3 by 2 cm. developed in a period of nine weeks.

In general, the prognosis is good. Of our 28 patients 4 died, 15 recovered completely, 3 are under treatment, and in 6 cases the results are indeterminate. One patient with multiple lesions has been followed for twenty-three years with no recurrence and for twenty years has been living a normal life without any residual effects of his disease. There has been no evidence to suggest mental deterioration in those patients who have been treated and recovered.

Age is apparently directly related to prognosis. The younger the child, the

poorer is the outlook. The reason for recovery in many cases and death in some is not clear. Evidence of replacement of hematopoietic tissue by the abnormal tissue of reticulo-endotheliosis has been found in some of the fatal cases.

SUMMARY

The roentgenograms in 28 cases of reticulo-endotheliosis have been reviewed with particular emphasis on the appearance of lesions of the skeleton and lungs.

There is little reason to consider Hand-Schüller-Christian disease, eosinophilic granuloma of bone, and Letterer-Siwe disease as separate entities. The pathologic and roentgenographic manifestations of these diseases are very similar.

Reticulo-endotheliosis is not an uncommon disease in children, and its early recognition may result in adequate treatment with a high percentage of complete recovery.

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SUMARIO

Retículo-Endoteliosis (Enfermedad de Hand-Schüller-Christian)

Un repaso de la literatura relativa a las afecciones del grupo retículo-endotelial—enfermedad de Hand-Schüller-Christian, enfermedad de Letterer-Siwe y granuloma eosinófilo de los huesos—va seguido de la descripción de 28 casos tratados en la Clínica Mayo. Hay pocos motivos para considerer dichos estados como entidades independientes, dado que son muy semejantes las manifestaciones patológicas y radiográficas.

De la serie de casos aquí comunicada, 16 fueron considerados como casos de la enfermedad de Hand-Schüller-Christian (incluso 3 diagnosticados clínicamente como casos de la enfermedad de Letterer-Siwe) y 5 como ejemplos de granuloma eosinófilo. La edad de los enfermos variaba de menos de un año a trece años. Diez eran asintomáticos. En el resto había presentes los siguientes signos y síntomas: exoftalmía, linfadenopatía, hepatomegalia, esplenomegalia, poliuria, lesiones cutáneas y manifestaciones pulmonares.

Las manifestaciones roentgenológicas de la retículo-endoteliosis en el esqueleto consisten en zonas de osteolisis, por lo general, aunque no siempre, múltiples. El cráneo es el invadido con mayor frecuencia, yendo seguido de los huesos pelvianos, fémur, costillas, húmero y omoplato. En los sujetos con invasión pulmonar, las radiografías torácicas muestran sombras nodulares algo tenues esparcidas por los pulmones a lo largo del trayecto de la marcas broncovasculares. Entre los estados que exigen diferenciación figuran las metástasis carcinomatosas, el mieloma múltiple y las lesiones esqueléticas localizadas, y notablemente meningiomas, quistes epidermoideos y osteomielitis en el cráneo y sarcoma de Ewing en los huesos largos.

En general, el pronóstico es favorable: 15 enfermos de la serie descrita se repusieron por completo; 3 estaban todavía en tratamiento; y en 6 el resultado era incierto. Hubo 4 muertes. Mientras más joven es el sujeto, menos favorable resulta el pronóstico.

Reticulo-Endotheliosis of Children: Treatment with Roentgen Rays[1]

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RETICULO-ENDOTHELIOSIS is characterized by the presence of collections of hyperplastic reticulo-endothelial cells in bone and soft tissue. Clinical and pathologic manifestations of this disease may vary, but three general types are recognized: Letterer-Siwe disease, Hand-Schüller-Christian disease, and eosinophilic granuloma of bone. Hodgson, Kennedy, and Camp (1) have pointed out the difficulty of assigning a particular case to a single category because a single patient may display characteristics of more than one type. This discussion will deal with cases of reticulo-endotheliosis which fit best into the category of Hand-Schüller-Christian disease.

Sosman (2), in 1930, reported 3 cases of Hand-Schüller-Christian disease in which treatment with roentgen rays was successful. Wallace (3), in 1949, stressed the important role of irradiation in control of this disease. Both Sosman and Wallace emphasized that there is a marked tendency to remission in reticulo-endotheliosis and that the role of irradiation therapy is to arrest progression of the disease, to prevent deformity, and possibly to induce remission.

However, the general impression still conveyed by most texts (4–7) on radiotherapy is that this disease is fatal, and the usefulness of ionizing radiations in its control does not seem to be generally recognized. It is the purpose of this paper to report the experience of the Mayo Clinic in the treatment by irradiation of reticulo-endotheliosis of children.

Twenty-eight children with reticulo-endotheliosis have been seen at this institution. Of these, 12 received a significant portion of their radiation therapy in the Section of Therapeutic Radiology and are the subjects of this report.[4]

The first patient of the series (Case 1, Table I), who was first seen in 1927, was treated with radium. Fifty milligrams of radium element, with filtration of 2 mm. lead and 1.5 mm. monel metal, were used at a distance of 2.5 cm. One-half to three-quarters of an erythema dose was delivered to the skin overlying each lesion, at intervals of from one to three months, from October 1927 to October 1928, with marked beneficial result. Fifteen years following the last treatment, the patient was normal in every respect and apparently free from disease.

The remainder of the patients received roentgen therapy under a fairly uniform technic. On the initial visit, the various lesions which had been identified on physical examination and in roentgenograms of the skeletal system were treated. The patients then were seen at intervals of from one to three months and an attempt was made to treat every lesion which appeared to be active at each visit. For superficial lesions of the soft tissue and for lesions of the skull, mandible, or long bones, a single portal over the affected region was used. For more deeply situated lesions, such as those of the pelvic bones or of the liver, spleen, or lungs, treatment was given through several portals (usually an anterior and a posterior). In the majority of cases a single dose of from 150 to 200 r, measured in air, was given at each portal. From one

[1] Presented at the Thirty-sixth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 10–15, 1950.

[2] Section of Therapeutic Radiology.

[3] Section of Pediatrics.

[4] Patients with solitary lesions and patients who received radiation therapy at other institutions are not included.

TABLE I: RETICULO-ENDOTHELIOSIS IN CHILDREN. SUMMARY OF CASES

Patient	Age (years)	Symptoms and Extent of Disease	Biopsy	Result
1	5/6	Exophthalmos; scalp tumors; defects of skull and long bones; anemia	None	Radium therapy 1927-1928. No evidence of disease after 15 years
2	3	Scalp tumor; skull defects	Xanthoma	Apparently free of disease
3	2	Lymphadenopathy; areas of destruction in skull and hip	Reticulo-endotheliosis, xanthoma	Free of disease
4	3	Staggering gait; fever; proptosis; cutaneous, skull, mandible, rib, and long bone lesions	Multiple myeloma,* xanthoma	Much x-ray treatment after dismissal in 1938. Alive in 1948
5	2	Lymphadenopathy; pulmonary involvement; multiple defects of skull and long bones	Xanthoma	Alive and well
6	2	Hepatomegaly, adenopathy, defects of skull and long bones. After 5 courses of treatment, anemia, leukopenia, thrombocytopenia, and death	Xanthoma with eosinophils and giant cells	Dead
7	3	Cervical and abdominal adenopathy; defects of skull and long bones	Eosinophilic granuloma	Last treatment 1945; accepted for life insurance 1949. Free of disease
8	4	Scalp tumors; defects in skull and femur	Xanthoma	Free of disease
9	3	Pelvic mass; hip lesion; tumor of occipital region; diabetes insipidus; multiple lesions of skull, mandible, and long bones	Eosinophilic granuloma	Disease apparently arrested; residual limp and underdeveloped femur
10	2	Draining ear; dermatitis; liver, spleen, and lymph nodes enlarged; dental involvement; extensive defects in skull and other bones; Hand-Schüller-Christian triad. After 10 courses of treatment leukopenia, anemia, thrombocytopenia, and death	Eosinophilic granuloma	Dead
11	4	Hand-Schüller-Christian triad; lesions in skull, mandible, ribs, pubis, femur	Eosinophilic granuloma*	Disease apparently arrested
12	2	Scalp tumor; exophthalmos; liver, spleen, and lymph nodes enlarged; pulmonary involvement. Defects in skull and long bones. After several courses of treatment, progressive leukopenia, anemia, thrombocytopenia, and death	Xanthoma	Dead

* Elsewhere.

to four portals were used daily. The technical factors were: 130 kv., half-value-layer 0.3 mm. copper, distance 40 cm. The estimated tumor dose per lesion per course of treatment was approximately 200 r.

SUMMARY OF CASES

A summary of the clinical and pathologic findings in the 12 cases is presented in Table I. All of the patients were four years of age or younger; 5 were two years old; 4 three years, 2 four years, and 1 was ten months of age.

Defects of the skull were present in every case; lesions of other bones were present in all but one. In 6 of the patients lymphadenopathy, hepatomegaly, or splenomegaly occurred. There were two instances of pulmonary involvement. In only 2 cases was the entire triad of diabetes insipidus, exophthalmos, and bone defects observed.

Nine of the 12 patients responded well to treatment and the disease is considered to be arrested. In the remaining 3 patients (Cases 6, 10, and 12) the condition progressed rapidly and death ensued.

The response to radiation therapy in most cases was prompt. The lesions of soft tissue and the enlargement of lymph nodes began to regress within ten days

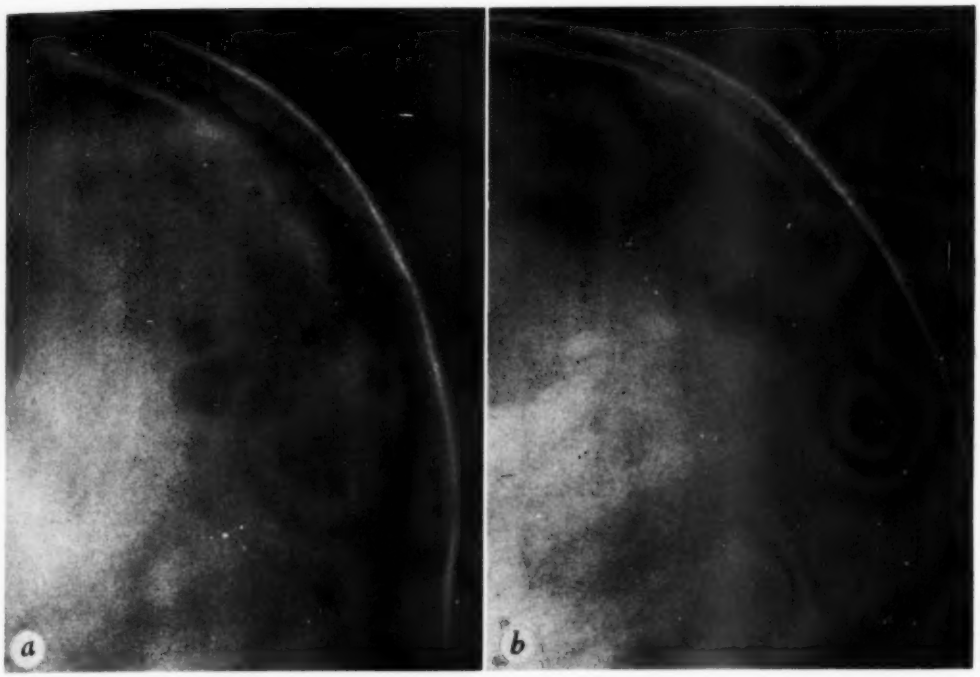

Fig. 1. Case 5. Areas of destruction in parieto-occipital region of skull, (*a*) before and (*b*) one month following treatment.

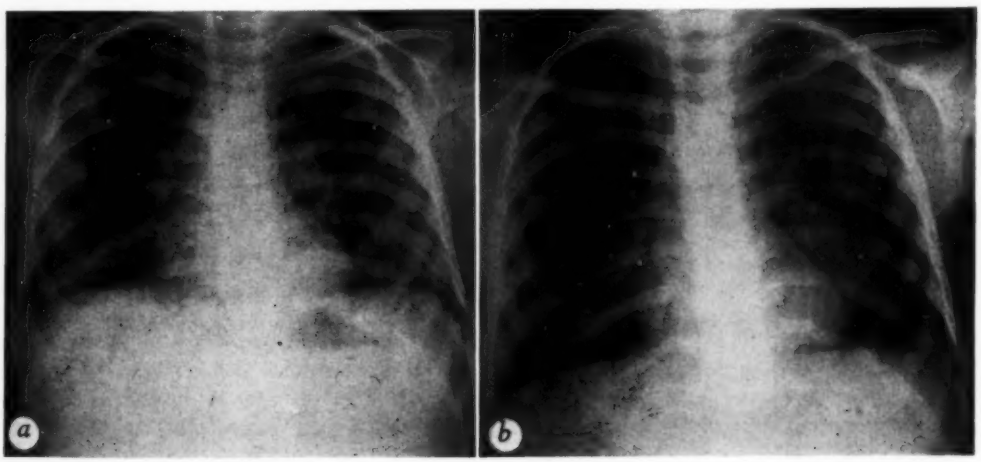

Fig. 2. Case 5. Thoracic roentgenograms, (*a*) before and (*b*) several years after treatment.

following treatment. Roentgenographic evidence of healing of the lesions of bone was seen by thirty days after the conclusion of irradition. In the majority of cases at least 3 courses of treatment (or a total of 600 r) were necessary to control any specific lesion. Figure 1 shows a lesion of the skull before treatment and one month after treatment. The characteristic appearance of the healing lesion is seen. New bone

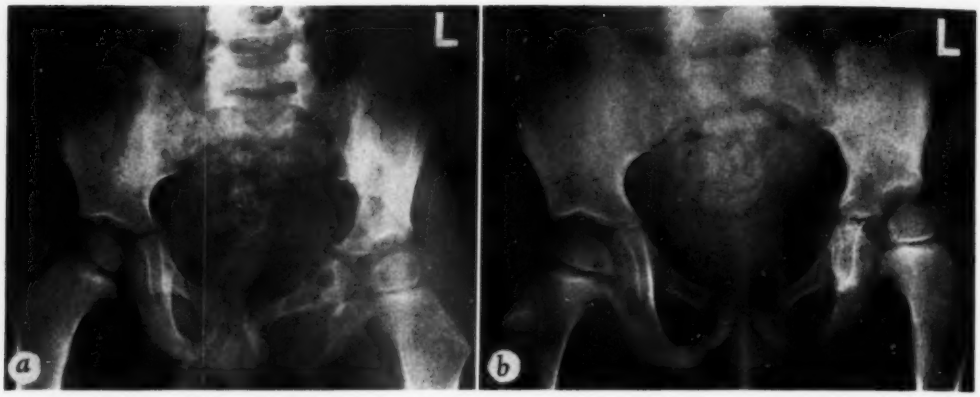

Fig. 3. Case 9. Destruction in the left innominate bone, (*a*) before and (*b*) two years following roentgen therapy.

fills in the defect, starting from the periphery and working towards the center of the lesion. Figure 2 represents a lesion of the lungs and its appearance following treatment.

ILLUSTRATIVE CASE

CASE 9: A boy three years of age was admitted to the Clinic Oct. 1, 1945. Nine months prior to admission he had begun to limp and his local physician had found a destructive lesion in the left hip. Traction had been maintained for about six months, with little benefit.

On admission to the Clinic, the boy appeared to be fairly healthy, although his limp was conspicuous. A firm pelvic mass, which appeared to be fixed to the sacrum, was palpable on rectal examination. A roentgenogram of the pelvis (Fig. 3*a*) disclosed a destructive lesion of the left innominate bone. The lesion was considered to be inoperable and the patient was referred for roentgen therapy.

Treatment was by way of two small anterior and two small posterior portals. Each portal received a dose (air) of 450 r. One month later the large pelvic mass was no longer palpable and a roentgenogram gave evidence of considerable healing of the destructive lesions. Treatment was repeated in November and December 1945. No further treatment was given to this region. Figure 3*b* shows the roentgenographic appearance in October 1947.

On one of the visits to the clinic, the child's mother called attention to a small nodule in the occipital region, and in June 1946, a biopsy specimen was taken at this site. The result was a diagnosis of eosinophilic granuloma. Roentgenograms of the skull at this time (Fig. 4*a* and *b*) gave evidence of a large lesion in the occipital region. This was treated through a single portal with a dose of 180 r in June and again in July 1946. In September of the same year the roentgenogram indicated that healing had begun.

In June 1947, diabetes insipidus developed and in October signs of destruction of the floor of the sella turcica were noted in the roentgenogram of the skull (Fig. 4*c*). At this time, right and left temporal portals each received 180 r and the treatment was repeated in October 1948. This was followed by healing of the sellar lesion and improvement of the diabetes.

In June 1948, evidence of destruction in the head of the right femur was found, but the process subsided after treatment. In October of the same year, a new lesion appeared in the occiput and dental involvement was noted. These lesions subsided after two treatments, given at an interval of one month, a dose of 180 r being delivered at each treatment.

The patient was last seen in September 1950, at which time there was no evidence of notable bony defects except for a lesion in the neck of the left femur, which apparently was arrested. No treatment was given at this time. The patient had rather a pronounced limp, attributable to underdevelopment of the left femur, as was evident on roentgenograms, and atrophy of the muscles of the left thigh. His intelligence quotient at this time was found to be within normal limits. A roentgenogram of the skull made in March 1950 is reproduced in Figure 4*d*.

COMMENT

The above case illustrates the typical course of reticulo-endotheliosis in children and its rapid and favorable response to treatment. Of particular interest is the onset, almost two years after discovery of the disease, of diabetes insipidus, accompanied by roentgenographic evidence of destruction in the sella turcica, and the

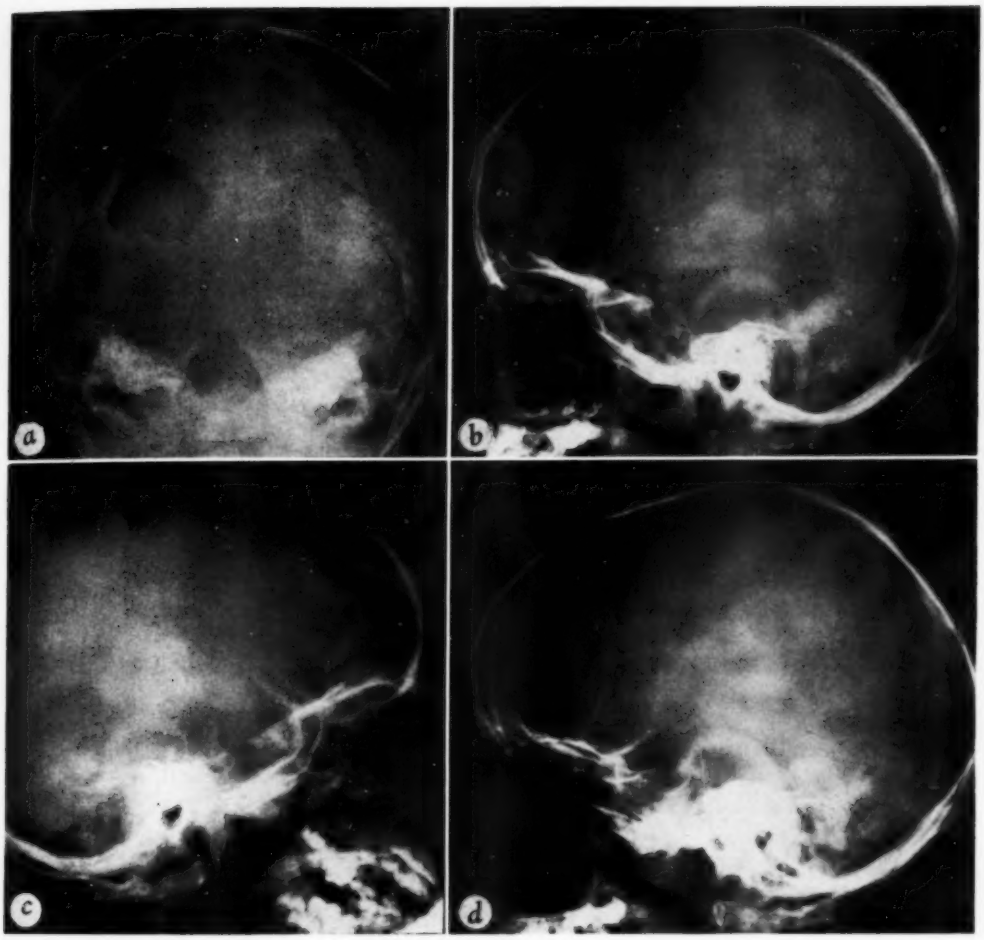

Fig. 4. Case 9. Anteroposterior (*a*) and lateral (*b*) roentgenograms of skull made in June 1946, before treatment, giving evidence of large defect in occipital bone. Lateral roentgenograms of skull, (*c*) at onset of diabetes insipidus in 1947; (*d*) in 1950.

disappearance of this sign following irradiation. The residual limp and undeveloped femur are undesirable sequelae of irradiation of growing bone; in this case the upper part of the femur received 1,700 r over a period of three months.

In Cases 6, 10, and 12 there was little evidence of healing of lesions following irradiation and, after several courses of treatment, leukopenia, anemia, and thrombocytopenia developed; the patients failed rapidly and died. In circumstances such as these, which include the presence of extensive disease and subjection of the patient to multiple courses of roentgen therapy, considerable speculation is aroused as to the role of irradiation in production of depression of the bone marrow. Each of these three patients died at home and autopsy was not done. A specimen of the bone marrow was obtained postmortem in Case 6 and showed evidence of replacement of the normal marrow with reticuloendothelial cells. It is possible, therefore, that the depression of bone marrow is caused by replacement of this kind as well as by irradiation.

The majority of the patients in this

series were treated with relatively low doses of roentgen rays (approximately 200 r per course), and no statement can be made as to the possibility of increased benefit from higher doses. In one of the fatal cases (Case 10) doses were in the neighborhood of 1,000 r before the child came to the Clinic. The bony lesions did not respond to this dosage or to the lower doses subsequently given. It should be stressed that in treating children with this disease the lower the dose of roentgen rays which can be used effectively, the less is the likelihood of damage to growing bones and teeth.

It is our opinion that irradiation therapy should be tried in all cases of reticuloendotheliosis. Several authors (6, 8, 9) have suggested that roentgen therapy is not indicated in Letterer-Siwe disease. The diagnosis of this latter disease may be difficult and may be established only postmortem. In the cases of this series in which death occurred (Cases 6, 10, and 12) splenomegaly or hepatomegaly, lymphadenopathy, and anemia were present in addition to bony defects; these cases may be considered to be in the category of Letterer-Siwe disease. In several other cases, however, which did not terminate fatally (Case 3, for instance) the findings were similar on admission and improvement was marked following roentgen therapy.

SUMMARY

Twelve children with extensive reticuloendotheliosis of the Hand-Schüller-Christian type were treated with multiple low doses of radiation. Three of the patients died of the disease; 9 recovered.

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SUMARIO

Retículo-Endoteliosis Infantil: Tratamiento con los Rayos X

Doce niños con retículo-endoteliosis extensa tipo Hand-Schüller-Christian fueron tratados con dosis bajas múltiples de irradiación. Un enfermo recibió la curieterapia; el resto, la roentgenoterapia. Para la última, los enfermos fueron atendidos a plazos de uno a tres meses, haciéndose un esfuerzo para tratar en cada ocasión toda lesión que parecía activa. Para las lesiones superficiales de los tejidos blandos y para las del cráneo, mandíbula o huesos largos, se empleó una sola puerta; para las más profundas, el tratamiento fué administrado a través de dos o más puertas. La mayoría de los pacientes recibieron una sola dosis de 150 a 200 r (al aire) por cada puerta, tratándose diariamente de una a cuatro puertas. Los factores fueron: 130 kv., capa de hemirreducción 0.3 mm. de cobre, distancia 40 cm. La dosis tumor calculada por lesión durante la serie fué de unos 200 r. Nueve de los sujetos respondieron bien al tratamiento y se considera que se ha estacionado la enfermedad. En 3 casos, hubo rápida agravación del mal, sobreviniendo la muerte.

DISCUSSION

(Papers by Hodgson, Kennedy, and Camp, and Childs and Kennedy)

Leo G. Rigler, M.D. (*Chairman*): Since reticulo-endotheliosis is predominantly a disease of childhood, it is appropriate that the presentation be continued by a distinguished pediatrician, and I am very happy to present Dr. Roger L. J. Kennedy of Rochester.

Roger L. J. Kennedy, M.D. (Rochester, Minn.): Two points concerning this discussion will bear emphasis: first, the material that has been presented refers to children, all the patients being under fifteen years of age, and second, statements which have been and are to be made are based only on material with which we have had experience.

Everyone here today has some knowledge of this disorder and each has been impressed by certain features. As a result, we have received impressions which we must be careful not to allow to become too fixed and to lead us to be dogmatic in our statements. Each of you, in discussing your experience with this condition, would be inclined to stress certain aspects that others of us have not encountered frequently and with which we have not been equally impressed.

I should like to tell you something about the first case that we observed. The child, aged ten months, had a downward and slightly outward displacement of one eye. Roentgenograms disclosed multiple areas of destruction in the skull and widespread involvement of many other bones. Since we were convinced that we were dealing with a generalized malignant process, a biopsy was considered unnecessary. At the request of the parents, treatment with radium was given. It was observed over a period of two or three years that the treated lesions did not enlarge further, that they tended to fill in, and that, while they were filling in, other lesions made an appearance. Although the outlook for a long time was considered hopeless, the child recovered. Some of the lesions undoubtedly underwent involution spontaneously, but the question was raised as to whether the involution might have been due in part to a remote effect of the treatment that was administered over other lesions. It has been recognized since then that some lesions do undergo involution and heal spontaneously. When the boy was five years of age the condition of the skeleton was good. There was a residue of a lesion in one ilium, but otherwise the bony architecture had returned practically to normal. It was a pleasure to have the boy stop in to say "hello" to us when he was sixteen years of age. He was at that time nearly 6 feet tall, and when he was seen recently his height had fully attained the 6-foot level and he was quite well in all respects.

It is probably unwise to use the term "typical" in speaking of any of the variations or examples of this disease. When one speaks of Hand-Schüller-Christian disease, one implies the presence of diabetes insipidus, exophthalmos, and defects in the skull, but any one or two of these features may be absent and the remaining feature or features may still be quite diagnostic if not actually "typical."

The histologic findings and the clinical features are so variable that any attempt to differentiate Hand-Schüller-Christian disease from eosinophilic granuloma or Letterer-Siwe disease seems to be impossible. We are inclined, therefore, to consider all of these cases as instances of a general group in which multiple manifestations are exhibited.

A rapid review of some of the histopathologic findings will emphasize the variability of microscopic appearances. As Dr. Childs pointed out, the pathologist may report that a biopsy reveals xanthomatosis or a picture that is consonant with what is called xanthomatosis or reticulo-endotheliosis.

Biopsy of the skull of one patient revealed many large, clear, fat-filled cells which are characteristic of xanthoma. This finding was repeated in several other patients. In another case a skull biopsy showed giant cells and a few foam cells. One child, aged two years and a half, had multiple lesions of the skeleton. The condition proved to be fatal. Histopathologic examination revealed giant cells and reticulo-endothelial cells with little if any connective tissue. The pathologist stated that the appearance was consistent with xanthoma. Another child, aged three years, had outward and downward displacement of one eye. Biopsy showed reticulo-endothelial cells and a few scattered eosinophilic cells, but in a different area of the section were many eosinophilic cells, so that there was a combination of eosinophils and reticulo-endothelial proliferation, components of so-called eosinophilic granuloma, in a child who had multiple lesions. Tissue from another child was of much the same appearance and again multiple lesions of the skeleton were present. A biopsy specimen from another young patient contained one cell which might have been a giant cell; the balance of the section was made up of degenerating cells that could not be said to be diagnostic of anything. A biopsy specimen from another child showed only complete necrosis in which there were what appeared to be cholesterin crystal clefts such as one might find in necrosis of many kinds of tissue.

All of the foregoing examples were observed in tissue that was removed from lesions of the skull. Biopsy specimens from elsewhere than the skull

also revealed a variety of appearances. In one which was taken from a lymph node of a patient with lesions in the skull, only reticulo-endothelial cells were found, which had led to a diagnosis of malignant reticuloma. The child, however, made a good recovery. A lymph node from another patient contained many eosinophils in a granuloma. It was a perfectly good example of eosinophilic granuloma, not of the bone but of a lymph node. There also was bony involvement. A biopsy specimen from a child who had multiple lesions showed foam cells but also a heavy infiltration of eosinophils. In another patient tissue from the humerus was characteristic of eosinophilic granuloma but the lesions were multiple and extensive, and death ensued. One patient who had multiple lesions in the skull and long bones consisting of reticulo-endothelial cells and giant cells had the same sort of tissue in the lungs and liver. This was a granuloma with very numerous large giant cells. Finally, a biopsy specimen from a child, aged eleven months, with multiple lesions of the skeleton, showed nothing but cellular debris.

Such variability in histopathologic appearances as well as variations in the clinical and roentgenologic features will account for different impressions and ideas, depending upon individual experience. Appreciation of the fact that the histopathologic appearance varies, possibly, as has been suggested, according to different phases of the disease, will explain the variability of biopsy reports. Judged by our experience, the uniformity and reliability of roentgenologic findings may be greater than of the pathologic findings as an aid to diagnosis.

Ross Golden, M.D. (New York): When you see the printed text of Dr. Hodgson's paper you will realize, as I do now (I have seen the manuscript), what an excellent job he and his coworkers have done in correlating and assembling information from the literature and from their own series of cases.

Personally I see no objection at the present time to the use of the term "reticulo-endotheliosis," for the reasons that he very ably showed. Until some information is obtained as to the possible etiology of this process I think that is a very good suggestion.

Dr. Rigler referred to the fact that this is predominantly a disease of childhood, but we must not forget that it occurs also in adults and we must bear it in mind under certain conditions. For example, I remember that we had, twenty-two years ago, a Greek waiter about thirty years old with a large destructive process in the os calcis which compelled him to discontinue his occupation. The biopsy showed it was a xanthoma. He got x-ray treatment with complete relief of his symptoms. His pain was so bad that he couldn't stand to have anybody touch the ankle at all.

And about ten years ago a forty-year-old woman with severe headache was found to have an area of diminished density in the lateral wall of the left orbit, the only lesion in her entire skeleton. The possibility of an eosinophilic granuloma was suggested as an explanation for this. Without a biopsy she was given x-ray treatment by Dr. Maurice Lenz and the headache promptly stopped, the lesion gradually disappeared, and she has been well now for nearly ten years.

So it is worth while to bear in mind that the same thing can happen to adults.

Dr. Childs has given us a very interesting summary of the experience at the Mayo Clinic in the x-ray treatment of these conditions and, in spite of the fact that it doesn't always work, it is a very valuable tool. I think it should be borne in mind that the treatment is being applied to a benign, not a malignant condition, and too much treatment should not be given.

I wish to compliment Dr. Hodgson and Dr. Childs on the excellence of their presentations.

W. Edward Chamberlain, M.D. (Philadelphia): I would like to add just one very small note. When we are dealing with a benign condition, one in which spontaneous regression may be hoped for, we must be particularly careful that the harmful effects of irradiation are kept to a minimum. Where the patient is small and a large proportion of the body is included in the beam, and where the total dose reaches a high figure through repeated treatments even though the individual doses are small, it certainly would be possible for aplastic anemia, which was the end-result in 3 cases in the series reported, to have been contributed to if not actually caused by irradiation.

The point I want to make is this: that in our anxiety to keep the dose down we may actually increase the total dose. We had an opportunity some years ago, in a series of 3 cases with multiple lesions, to try out different intensities, different total doses, and different fractionations on individual lesions and we established to our own satisfaction, as far as it could be established on about twenty lesions in 3 patients, that if you give 300 r into the lesion—not 300 r in the surface or in the air but in the lesion—there's a pretty good chance that further treatment will not be required, whereas if you give 200 r or less in the lesion you will almost surely have to retreat it, possibly several times.

We may actually cut down the harmful effects of irradiation by giving an adequate dose once and then waiting long enough to see whether the lesion does actually regress from a single treatment, which in our hands it did a number of times. And, of course, I think that we ought to remember that it doesn't take an awful lot of x-ray to produce a lot of harm if the entire patient is involved in the irradiation or if the spleen is included.

Pelvic Dimensions in Eutocia and Dystocia[1]

PAUL C. HODGES, M. D., and RUSSELL L. NICHOLS, M. D.
Chicago, Ill.

IN AN EARLIER paper in this journal, we have described a method for measuring the maternal pelvis by means of true dimensional tracings or orthograms that portray the mid-sagittal plane and the inlet, mid-pelvis, and outlet. For obstetrical hospitals or other institutions having a good deal of pelvimetry to do, the objective precision of the orthographic method is desirable and the cost not prohibitive; but in other situations, where the volume of work does not warrant the purchase of a 90° table and a pantograph, equally precise work may be done with simple inexpensive apparatus, provided the radiologist exercises skill and care in making and working up the roentgenographs.

The present paper is concerned with the clinical and roentgenological findings in 912 primiparous white women who were studied throughout pregnancy, including delivery. It had been our hope to report on an even thousand but 88 records had to be excluded, in most instances because the patient could not be followed through delivery. The work was done at the Chicago Lying-In Hospital of The University of Chicago, with the aid of Dr. M. E. Davis and presently will be published in detail in the obstetrical literature.

CLINICAL DATA

All of the patients were examined with particular care by our obstetrical colleague, a special record sheet being employed for listing normal and instrumental pelvimetry, a clinical estimate of the adequacy of the pelvis, the course and outcome of the labor, and the condition, weight, and degree of head moulding in the newborn infant. The labors were classified as short (less than twelve hours), medium (less than twenty-four hours), long (more than twenty-four hours), and section.

It had been planned to include caliper measurement of the fetal skull, but after the first few cases it was found preferable to substitute x-ray measurement during the first twenty-four hours of life—not only of the skull but of the trunk and extremities as well. In another publication we will weigh the relationship between pelvic dimensions and the ease or difficulty of labor against the dimensions of the fetus. The work-up of these data is not yet complete, but it is our impression that easy labor with small pelvic dimensions and difficult labor with pelvic diameters well above average are not the result of a small baby in the first instance or of a large one in the second instance.

DIMENSIONS AND INDICES

We have measured numerous pelvic diameters and computed numerous indices based on them. Of these, six diameters and three indices are presented in the accompanying tabular material. The reference points for these diameters and the nature of the indices are as follows:

Pelvic Inlet

Anteroposterior Diameter: The anterior end-point of this diameter is that point on the posterior surface of the pubic symphysis that lies nearest to the sacrum, and the posterior end-point is that point on the anterior surface of the sacrum that lies nearest to the pubis. Usually the posterior end-point is the promontory.

Transverse Diameter: This is the transverse diameter of the brim at its widest point.

Product Index of Inlet: This is the prod-

[1] From the Section of Radiology, University of Chicago, Chicago, Ill. Presented at the Thirty-sixth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 5-10, 1950.
This work has been aided by a grant from the State of Illinois Department of Public Health.

TABLE I: ANTEROPOSTERIOR DIAMETER OF INLET

Numerical Value of Diameter ±0.15 cm.	Outcome of Labor									
	All Types of Labor		Short Less than 12 hr.		Medium Less than 24 hr.		Long More than 24 hr.		Section	
	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage
8.5	1	0.11	0	0.00	0	0.00	0	0.00	1	3.03
9.7	4	0.55	0	0.00	2	0.80	2	3.85	0	3.03
10.0	4	0.99	1	0.17	2	1.61	0	3.85	1	6.06
10.3	16	2.74	7	1.38	4	3.21	1	5.77	4	18.18
10.6	22	5.15	11	3.29	7	6.02	2	9.62	2	24.24
10.9	49	10.53	31	8.65	11	10.44	6	21.15	1	27.27
11.2	50	16.01	29	13.67	15	16.47	6	32.69	0	27.27
11.5	97	26.64	65	24.91	25	26.51	4	40.39	3	36.36
11.8	114	39.14	74	37.71	32	39.36	2	44.23	6	54.55
12.1	150	55.59	97	54.50	37	54.22	10	63.46	6	72.73
12.4	120	68.75	75	67.47	32	67.07	7	76.92	6	90.91
12.7	95	79.17	64	78.54	25	77.11	5	86.54	1	93.94
13.0	73	87.17	54	87.88	17	83.93	1	88.46	1	96.97
13.3	47	92.33	29	92.90	13	89.16	4	96.16	1	100.00
13.6	26	95.18	11	94.80	15	95.18	0	96.16		
13.9	20	97.37	15	97.40	4	96.79	1	98.08		
14.2	14	98.90	9	98.96	4	98.39	1	100.00		
14.5	7	99.67	4	99.65	3	99.60				
14.8	1	99.78	0	99.65	1	100.00				
15.1	1	99.89	1	99.82						
15.4	1	100.00	1	100.00						
NUMBER OF CASES	912		578		249		52		33	
ARITHMETIC MEAN OF DIAMETER	12.17		12.22		12.20		11.90		11.61	

TABLE II: TRANSVERSE DIAMETER OF INLET

Numerical Value of Diameter ±0.15 cm.	Outcome of Labor									
	All Types of Labor		Short Less than 12 hr.		Medium Less than 24 hr.		Long More than 24 hr.		Section	
	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage
10.9	1	0.11	0	0.00	1	0.40	0	0.00	0	0.00
11.2	4	0.55	2	0.35	1	0.80	1	1.92	0	0.00
11.5	12	1.86	9	1.90	3	2.01	0	1.92	0	0.00
11.8	23	4.39	15	4.50	5	4.02	1	3.85	2	6.06
12.1	67	11.73	50	13.15	9	7.63	4	11.54	4	18.18
12.4	74	19.85	36	19.38	31	20.08	3	17.31	4	30.30
12.7	130	34.10	82	33.56	36	34.54	8	32.69	4	42.42
13.0	155	51.10	98	50.52	46	53.01	4	40.39	7	63.64
13.3	162	68.86	102	68.16	38	68.27	16	71.15	6	81.82
13.6	122	82.24	79	81.83	31	80.72	8	86.54	4	93.94
13.9	68	89.69	44	89.44	20	88.75	4	94.23	0	93.94
14.2	55	95.72	35	95.50	17	95.58	2	98.08	1	96.97
14.5	26	98.58	18	98.61	7	98.39	1	100.00	0	96.97
14.8	7	99.34	4	99.30	2	99.20			1	100.00
15.1	4	99.78	3	99.82	1	99.60				
15.4	1	99.89	1	100.00	0	99.60				
16.6	1	100.00			1	100.00				
NUMBER OF CASES	912		578		249		52		33	
ARITHMETIC MEAN OF DIAMETER	13.13		13.13		13.15		13.12		12.93	

TABLE III: PRODUCT INDEX OF INLET

Index ±2.5	Outcome of Labor									
	All Types of Labor		Short Less than 12 hr.		Medium Less than 24 hr.		Long More than 24 hr.		Section	
	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage
105	1	0.11	0	0.00	0	0.00	0	0.00	1	3.03
110	1	0.22	0	0.00	0	0.00	1	1.92	0	3.03
115	0	0.22	0	0.00	0	0.00	0	1.92	0	3.03
120	5	0.77	2	0.35	2	0.80	0	1.92	1	6.06
125	6	1.43	5	1.21	1	1.20	0	1.92	0	6.06
130	19	3.51	10	2.94	4	2.81	2	5.77	3	15.15
135	31	6.91	19	6.23	7	5.62	2	9.62	3	24.24
140	57	13.16	29	11.24	22	14.46	5	19.23	1	27.27
145	81	22.04	52	20.24	18	21.69	7	32.69	4	39.39
150	98	32.79	57	30.10	32	34.54	6	44.23	3	48.48
155	113	45.18	78	43.60	26	44.98	5	53.85	4	60.61
160	117	58.00	74	56.40	32	57.83	8	69.23	3	69.70
165	99	68.86	66	67.82	25	67.87	3	75.00	5	84.85
170	97	79.50	66	79.23	24	77.51	3	80.77	4	96.97
175	69	87.06	44	86.85	21	85.94	3	86.54	1	100.00
180	60	93.64	41	93.94	14	91.56	5	96.16		
185	25	96.38	16	96.71	7	94.38	2	100.00		
190	13	97.81	8	98.09	5	96.38				
195	7	98.58	2	98.44	5	98.39				
200	5	99.12	3	98.96	2	99.20				
205	4	99.56	3	99.48	1	99.60				
210	1	99.67	1	99.65	0	99.60				
215	1	99.78	1	99.82	0	99.60				
220	1	99.89	1	100.00	0	99.60				
240	1	100.00			1	100.00				
NUMBER OF CASES	912		578		249		52		33	
ARITHMETIC MEAN OF INDEX	159.81		160.43		160.38		155.96		150.61	

uct of the anteroposterior diameter and the transverse diameter. It proves to be a useful value in spite of the fact that it is arbitrary, does not represent the area of the inlet plane, and should not be expressed in square centimeters.

Mid Pelvis

Anteroposterior Diameter: This is the sum of the anterior sagittal and the posterior sagittal of the mid pelvis and frequently it is an obtuse angle rather than an approximately straight line. The anterior end-point is that point on the posterior surface of the pubic symphysis that lies nearest to the interspinous diameter. The posterior end-point is that point on the anterior surface of the sacrum that lies nearest to the interspinous diameter. The intermediate point is the intersection of the interspinous diameter with the mid-sagittal plane.

Transverse Diameter: This is the interspinous diameter or, in other words, the distance between the two ischial spines.

Product Index: This is the product of the anteroposterior diameter and the transverse diameter of the mid pelvis.

Outlet

Anteroposterior Diameter: This is the sum of the anterior and posterior sagittals of the outlet and invariably is an obtuse angle, never a straight line. The anterior end-point is that point on the posterior surface of the pubic symphysis that lies nearest to the intertuberous diameter. The posterior end-point is that point on the anterior surface of the sacrum that lies nearest to the intertuberous diameter. The intermediate point is the intersection of the intertuberous diameter with the mid-sagittal plane.

TABLE IV: ANTEROPOSTERIOR DIAMETER OF MID PELVIS

Numerical Value of Diameter ±0.15 cm.	Outcome of Labor: All Types of Labor		Short Less than 12 hr.		Medium Less than 24 hr.		Long More than 24 hr.		Section	
	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage
8.9	1	0.11	0	0.00	0	0.00	0	0.00	1	3.03
9.2	8	0.99	3	0.52	4	1.61	1	1.92	0	3.03
9.5	20	3.18	12	2.60	4	3.21	3	7.69	1	6.06
9.8	27	6.14	17	5.54	8	6.43	2	11.54	0	6.06
10.1	39	10.42	30	10.73	5	8.43	2	15.38	2	12.12
10.4	70	18.09	39	17.47	22	17.27	4	23.08	5	27.27
10.7	91	28.07	59	27.68	25	27.31	4	30.77	3	36.36
11.0	111	40.24	66	39.10	31	39.76	10	50.00	4	48.48
11.3	120	53.40	77	52.42	27	50.60	9	67.31	7	69.70
11.6	122	66.78	82	66.61	31	63.05	6	78.85	3	78.79
11.9	99	77.63	60	76.99	31	75.50	6	90.39	2	84.85
12.2	78	86.18	47	85.12	27	86.35	3	96.16	1	87.88
12.5	59	92.65	42	92.39	14	91.97	1	98.08	2	93.94
12.8	23	95.18	12	94.46	9	95.58	1	100.00	1	96.97
13.1	18	97.15	13	96.71	4	97.19			1	100.00
13.4	12	98.47	7	97.92	5	99.20				
13.7	7	99.23	6	98.96	1	99.60				
14.0	6	99.89	5	99.83	1	100.00				
14.3	0	99.89	0	99.83						
14.6	1	100.00	1	100.00						
NUMBER OF CASES	912		578		249		52		33	
ARITHMETIC MEAN OF DIAMETER	11.38		11.41		11.41		11.09		11.14	

TABLE V: TRANSVERSE DIAMETER OF MID PELVIS

Numerical Value of Diameter ±0.15 cm.	Outcome of Labor: All Types of Labor		Short Less than 12 hr.		Medium Less than 24 hr.		Long More than 24 hr.		Section	
	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage
7.0	1	0.11	0	0.00	0	0.00	0	0.00	1	3.03
8.5	3	0.44	1	0.17	2	0.80	0	0.00	0	3.03
8.8	7	1.21	5	1.04	2	1.61	0	0.00	0	3.03
9.1	14	2.74	7	2.25	4	3.21	1	1.92	2	9.09
9.4	26	5.59	17	5.19	5	5.22	2	5.77	2	15.15
9.7	60	12.17	35	11.25	20	13.25	4	13.46	1	18.18
10.0	105	23.68	65	22.49	24	22.89	8	28.85	8	42.42
10.3	130	37.94	83	36.85	37	37.75	5	38.46	5	57.58
10.6	133	52.52	86	51.73	37	52.61	7	51.92	3	66.67
10.9	158	69.85	99	68.86	43	69.88	10	71.15	6	84.85
11.2	112	82.13	68	80.62	36	84.34	5	80.77	3	93.94
11.5	70	89.80	45	88.41	18	91.57	7	94.23	0	93.94
11.8	44	94.63	30	93.60	11	95.98	1	96.16	2	100.00
12.2	19	96.71	16	96.37	2	96.79	1	98.08		
12.4	20	98.90	13	98.62	6	99.20	1	100.00		
12.7	5	99.45	5	99.48	0	99.20				
13.0	1	99.56	0	99.48	1	99.60				
13.3	4	100.00	3	100.00	1	100.00				
NUMBER OF CASES	912		578		249		52		33	
ARITHMETIC MEAN OF DIAMETER	10.70		10.73		10.68		10.66		10.29	

TABLE VI: PRODUCT INDEX OF MID PELVIS

Index ±2.5	Outcome of Labor									
	All Types of Labor		Short Less than 12 hr.		Medium Less than 24 hr.		Long More than 24 hr.		Section	
	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage
75	1	0.11	0	0.00	0	0.00	0	0.00	1	3.03
80	0	0.11	0	0.00	0	0.00	0	0.00	0	3.03
85	3	0.44	1	0.17	1	0.40	0	0.00	1	6.06
90	6	1.10	3	0.69	1	0.80	2	3.85	0	6.06
95	28	4.17	16	3.46	6	3.21	2	7.70	4	18.18
100	36	8.11	22	7.27	10	7.23	1	9.62	3	27.27
105	73	16.12	43	14.71	20	15.26	7	23.08	3	36.36
110	93	26.32	64	25.78	22	24.10	5	32.69	2	42.42
115	125	40.02	76	38.93	37	38.96	10	51.92	2	48.48
120	139	55.26	88	54.15	40	55.02	5	61.54	6	66.67
125	110	67.33	74	66.95	28	66.27	3	67.31	5	81.82
130	114	79.83	69	78.89	34	79.92	9	84.62	2	87.88
135	80	88.60	47	87.02	22	88.76	7	98.08	4	100.00
140	40	92.98	28	91.87	12	93.58	0	98.08		
145	25	95.72	21	95.50	4	95.18	0	98.08		
150	19	97.81	10	97.23	8	98.39	1	100.00		
155	11	99.01	8	98.62	3	99.60				
160	4	99.45	3	99.13	1	100.00				
165	1	99.56	1	99.31						
170	3	99.89	3	99.83						
175	1	100.00	1	100.00						
NUMBER OF CASES	912		578		249		52		33	
ARITHMETIC MEAN OF INDEX	121.40		122.02		121.67		118.17		113.64	

Transverse Diameter: This is the intertuberous diameter or, in other words, the distance between the medial surfaces of the two ischial tuberosities.

Product Index: This is the product of the anteroposterior diameter and the transverse diameter of the outlet.

Numerical Values

The values of these nine diameters and indices classified by the outcome of labor are listed in Tables I to IX. Table I deals with the anteroposterior diameter of the inlet, Table II with the transverse diameter of the inlet, Table III with the product index of the inlet. Tables IV, V, and VI show the values of the diameters and index of the mid pelvis, and Tables VII, VIII, and IX those of the outlet.

Each table is divided into 11 vertical columns. Column 1 shows the numerical values of the diameters and indices sorted into groups over a ± range that varies from 0.15 cm. to 0.25 cm. in the case of the diameters and from 2.5 to 3.5 arbitrary units in the case of the indices. Column 2 shows the number of cases in each group, and column 3 the cumulative percentage for each group. For example, in Table I, which deals with the anteroposterior diameter of the inlet, we learn from the figures in the eighth horizontal row, in columns 1, 2, and 3, that there were 97 cases in which the anteroposterior diameter of the inlet ranged from 11.35 to 11.65 cm. (that is, the value was 11.5 cm. ± 0.15 cm.) and that 26.6 per cent of the cases in the entire series had anteroposterior inlet diameters at or below this value. In all of the tables, columns 4 and 5 indicate the number of cases for each diameter or index group and the cumulative percentage for each group in the 578 cases with short labors. Columns 6 and 7 show these same values for the 249 cases with medium length labors; columns 8 and 9 for the 52 instances of

TABLE VII: ANTEROPOSTERIOR DIAMETER OF OUTLET

(Sum of Anterior and Posterior Sagittals)

Numerical Value of Diameter ±0.25 cm.	Outcome of Labor									
	All Types of Labor		Short Less than 12 hr.		Medium Less than 24 hr.		Long More than 24 hr.		Section	
	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage
9.0	1	0.11	1	0.17	0	0.00	0	0.00	0	0.00
10.0	2	0.33	2	0.52	0	0.00	0	0.00	0	0.00
10.5	9	1.32	5	1.38	3	1.20	0	0.00	1	3.03
11.0	21	3.62	14	3.81	5	3.21	0	0.00	2	9.09
11.5	32	7.13	17	6.75	10	7.23	4	7.70	1	12.12
12.0	51	12.72	37	13.15	10	11.25	2	11.54	2	18.18
12.5	87	22.26	52	22.15	23	20.48	8	26.92	4	30.30
13.0	112	34.54	71	34.43	28	31.73	9	44.23	4	42.42
13.5	133	49.12	88	49.65	33	44.98	10	63.46	2	48.48
14.0	144	64.91	84	64.19	42	61.85	9	80.77	9	75.76
14.5	118	77.85	77	77.51	34	75.50	3	86.54	4	87.88
15.0	95	88.27	60	87.89	28	86.75	5	96.16	2	93.94
15.5	56	94.41	37	94.29	16	93.17	1	98.08	2	100.00
16.0	28	97.48	17	97.23	10	97.19	1	100.00		
16.5	15	99.12	9	98.79	6	99.60				
17.0	8	100.00	7	100.00	1	100.00				
NUMBER OF CASES	912		578		249		52		33	
ARITHMETIC MEAN OF DIAMETER	13.73		13.74		13.83		13.42		13.39	

TABLE VIII: TRANSVERSE DIAMETER OF OUTLET

(Intertuberous Diameter)

Numerical Value of Diameter ±0.15 cm.	Outcome of Labor									
	All Types of Labor		Short Less than 12 hr.		Medium Less than 24 hr.		Long More than 24 hr.		Section	
	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage
7.8	2	0.22	1	0.17	1	0.40	0	0.00	0	0.00
8.1	0	0.22	0	0.17	0	0.40	0	0.00	0	0.00
8.4	4	0.66	2	0.52	2	1.20	0	0.00	0	0.00
8.7	6	1.32	4	1.21	1	1.61	0	0.00	1	3.03
9.0	10	2.41	7	2.42	3	2.81	0	0.00	0	3.03
9.3	22	4.82	18	5.54	2	3.61	1	1.92	1	6.06
9.6	21	7.13	13	7.79	5	5.62	2	5.77	1	9.09
9.9	41	11.62	15	10.38	14	11.25	4	13.46	8	33.33
10.2	65	18.75	37	16.78	22	20.08	4	21.15	2	39.39
10.5	80	27.52	49	25.26	23	29.32	5	30.77	3	48.48
10.8	100	38.49	60	35.64	31	41.77	6	42.31	3	57.58
11.1	103	49.78	76	48.79	24	51.41	2	46.15	1	60.61
11.4	115	62.39	71	61.07	34	65.06	5	55.77	5	75.76
11.7	101	73.47	61	71.63	29	76.71	8	71.15	3	84.85
12.0	71	81.25	47	79.76	14	82.33	8	86.54	2	90.91
12.3	62	88.05	45	87.54	14	87.95	3	92.31	0	90.91
12.6	41	92.54	23	91.52	13	93.17	3	98.08	2	96.97
12.9	33	96.16	24	95.67	9	96.79	0	98.08	0	96.97
13.2	19	98.25	14	98.10	4	98.39	1	100.00	0	96.97
13.5	10	99.34	7	99.31	3	99.60			0	96.97
13.8	5	99.89	3	99.83	1	100.00			1	100.00
14.4	1	100.00	1	100.00						
NUMBER OF CASES	912		578		249		52		33	
ARITHMETIC MEAN OF DIAMETER	11.24		11.28		11.19		11.21		10.83	

TABLE IX: PRODUCT INDEX OF OUTLET

Index ±3.5	Outcome of Labor									
	All Types of Labor		Short Less than 12 hr.		Medium Less than 24 hr.		Long More than 24 hr.		Section	
	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage	No. of Cases	Cumulative Percentage
95	1	0.11	1	0.17	0	0.00	0	0.00	0	0.00
102	4	0.55	2	0.52	2	0.80	0	0.00	0	0.00
109	12	1.86	9	2.08	1	1.20	0	0.00	2	6.06
116	25	4.61	16	4.84	5	3.21	1	1.92	3	15.15
123	43	9.32	22	8.65	15	9.24	3	7.69	3	24.24
130	55	15.35	41	15.74	9	12.85	4	15.38	1	27.27
137	96	25.88	59	25.95	28	24.10	8	30.77	1	30.30
144	101	36.95	52	34.95	34	37.75	8	46.15	7	51.52
151	124	50.55	83	49.31	29	49.40	7	59.62	5	66.67
158	117	63.38	74	62.11	35	63.45	3	65.39	5	81.82
165	109	75.33	69	74.05	29	75.10	6	76.92	5	96.97
172	87	84.87	49	82.53	28	86.35	10	96.16	0	96.97
179	69	92.43	55	92.04	12	91.17	2	100.00	0	96.97
186	28	95.51	17	94.98	11	95.58			0	96.97
193	22	97.92	15	97.58	7	98.39			0	96.97
200	9	98.90	7	98.79	1	98.80			1	100.00
207	7	99.67	4	99.48	3	100.00				
214	2	99.89	2	99.83						
221	0	99.89	0	99.83						
228	1	100.00	1	100.00						
NUMBER OF CASES	912		578		249		52		33	
ARITHMETIC MEAN OF INDEX	154.29		154.96		154.68		151.00		144.85	

long labor; columns 10 and 11 for the 33 cases that were delivered by section.

For this entire series of 912 primiparous white women the mean values for the nine diameters and indices are as follows:

Inlet: A.P. 12.17, T.D. 13.13, Index 159.8
Mid Pelvis: A.P. 11.38, T.D. 10.7, Index 121.4
Outlet: A.P. 13.73, T.D. 11.24, Index 154.2

For what it may be worth, our present opinion is that the three indices are the best guide to the dimensional adequacy of the maternal pelvis. We are conducting a statistical analysis of our measurements of these and several other dimensions and indices and when that work has been completed our opinion may have to be changed.

SMALLNESS OF RADIATION HAZARD

Our method of pelvimetry requires the making of two 10 × 12-inch films, one a frontal, the other a lateral. We estimate that in the making of the frontal film the skin of the maternal anterior abdominal wall receives an average dose of 2.5 r to a 7 × 8.5-inch portal and the fetus an average dose of 0.3 r. For the lateral film the corresponding doses are: to the skin at the side of the maternal abdomen 33 r to a 6 × 7.15-inch portal, and to the fetus 2.3 r. Of course, much larger doses would be tolerated without demonstrable damage.

CONCLUSIONS

There is such a thing as dystocia caused by deformity or smallness of the pelvic bones and radiology is by far the best means of determining whether those conditions are present. It is a safe means, too. But there are dystocias of many sorts, and it is rash indeed for the radiologist to assure the obstetrician that this woman will deliver easily, that one with difficulty or not at all.

The obstetrician who understands x-ray pelvimetry will employ it whenever the physical examination or history suggests the possibility of deficient pelvic dimen-

sions. If the radiologist reports indices at or above the mean value, he will be inclined to allow a labor to continue even though progress is slow, secure in the knowledge that the fetus will not encounter mechanical obstacles in its descent through the birth canal; but if the indices are well below mean, usually he will allow a test of labor only if the baby is small and the uterine contractions strong.

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SUMARIO

Las Dimensiones de la Pelvis en la Eutocia y la Distocia

Este trabajo está dedicado a los hallazgos clínicos y roentgenológicos en 912 primíparas blancas que fueron estudiadas durante todo el embarazo, el parto inclusive. Midiéronse numerosos conductos pelvianos y computáronse muchos índices. Las tablas correlacionan el resultado del parto con nueve de dichas mediciones: diámetros anteroposteriores y transversos del estrecho superior, pelvis media y estrecho inferior, y los índices respectivos (el producto de los diámetros conjugado y transverso).

Los AA. consideran dichos tres índices como el mejor guía para determinar la suficiencia dimensional de la pelvis materna.

El tocólogo familiarizado con la pelvimetría roentgenológica la empleará siempre que el examen físico o la anamnesia denoten la posibilidad de que sean deficientes las dimensiones pélvicas. Si los índices llegan a, o pasan de, la cifra media, se inclinará a dejar que prosiga el parto, aunque la evolución sea lenta, por abrigar la seguridad de que el feto no encontrará obstáculos mecánicos en su descenso por el conducto uterino, pero si los índices quedan bien por debajo del promedio, por lo general no permitirá un ensayo del parto a menos que la criatura sea pequeña y las contracciones uterinas sean poderosas.

Hepatolienography: Past, Present, and Future[1]

SYDNEY F. THOMAS, M.D., GEORGE W. HENRY, M.D., and HENRY S. KAPLAN, M.D.

THE LIVER AND SPLEEN are among the few structures in the body for which safe and reliable primary contrast roentgen diagnostic procedures have not been established. Hepatolienography with colloidal thorium dioxide[2] has been widely performed for many years (65), but this material has fallen into disfavor with many workers, though not all, as a result of a number of cases in which injurious effects presumably related to its use have been reported. Since thorotrast has been in clinical use for over twenty years, there is available a rather large body of pathological and clinical material in which its long-term effects may be studied. It has seemed desirable to attempt an evaluation of these effects, to formulate criteria for an ideal medium for opacification of the liver and spleen, and to report preliminary studies with other media.

I. EVALUATION OF THE EFFECTS OF THOROTRAST

Thorotrast is a 25 per cent suspension of thorium dioxide (15 to 20 per cent by weight) with an average particle size of 3 to 10 millimicrons by electron microscope measurements (38).

In colloidal suspension thorium dioxide is highly radiopaque, and satisfactory opacification of the liver and spleen is obtained with concentrations of less than 1 gm. of thorium dioxide per 100 gm. of wet tissue. The particulate matter is taken up by the reticulo-endothelial cells of the body and accumulates in the liver and spleen and to a lesser degree in the reticulo-endothelial system throughout the lymphatic, respiratory, and hemopoietic system.

Immediate Side Effects

Reactions during injection of thorotrast have been reported, although they are rather infrequent. These include mild fever lasting up to twenty-four hours, vomiting, anaphylactoid phenomena, exacerbation of asthma, transient anemia, leukopenia and relative lymphocytosis (65). Hematemesis has been reported in three patients with cirrhosis of the liver (89). In a patient observed by one of us (S. F. T.) generalized petechiae appeared following the injection of thorium dioxide (possibly due to the use of outdated thorotrast).

Late Effects

The late effects may be classified under two general headings: (A) possible induction of neoplasms and (B) local fibrosis at the site of injection or deposition. Thorium is radioactive, yielding alpha and gamma rays predominantly (77–79). The diagnostic dose of 75 c.c. of thorotrast is roughly equivalent to 3 micrograms of radium salt (18). Bone atrophy and necrosis and other late sequelae (anemia, etc.) have been reported with as little as 1 microgram of radium deposited in the body (51, 52).

Ionizing radiation in suitable doses is known to be capable of producing a number of late injurious effects. These include local necrosis (58) and fibrosis (1), the induction of malignant neoplasms in a variety of tissues (3, 8, 15, 16, 57, 67, 73, 83), and hemopoietic derangements (12, 34, 45, 46, 50, 69, 83, 84). The principal radiation effects with which we need to concern ourselves in the case of thorotrast

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[1] From the Department of Radiology, Stanford University School of Medicine, San Francisco, Calif. Presented at the Thirty-sixth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 10–15, 1950.

[2] Colloidal thorium dioxide has been marketed for many years under the name Thorotrast by the Heyden Chemical Corporation, New York. Dr. Charles Mann of that company has been most helpful in this investigation.

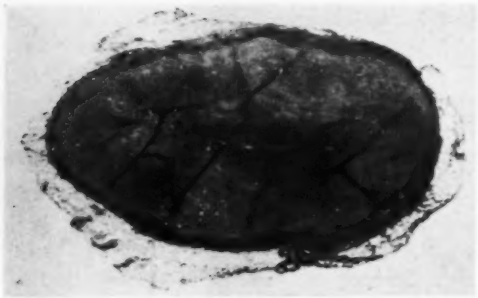


Fig. 1. Lymph node from the hilus of the liver of a patient who had received thorotrast six years earlier. Obliteration of the lymphoid elements is almost complete, with replacement by fibrous tissue. (See Table I)

are the development of malignant neoplasms and necrosis and fibrosis in organs where deposits of the material are heavy (23, 24, 26, 27, 44, 47, 64, 66, 68, 72, 81, 85).

A. Carcinogenicity: On a review of the literature and unpublished sources, at least five instances of malignant disease have been found in patients who previously received thorium dioxide: 1 published (49) and 2 unpublished cases of malignant tumor of the liver (see Fig. 3), a sarcoma of the kidney (90; *cf.* 91), and an unpublished case of leukemia (74; *cf.* 83). It seems probable that other instances have occurred which have not been published. (All are *post hoc* but not necessarily *propter hoc.*) In view of the long standing and widespread use of thorium dioxide, this low incidence of malignant neoplasms does not support the view that the material is carcinogenic in man. However, spontaneous selection of cases and the possibility that the period of observation has not been long enough must be considered. Tumor induction has been reported in animals after injection of colloidal thorium dioxide (57, 67), but Selbie pointed out that in mice, if the observation period were insufficient, this effect might not be observed (70). Erf suggested that in man about thirty years would be equivalent to the interval in some of the animal experiments (22). Bauer on the other hand suggests that twelve to eighteen years is an adequate latent period (2).

The amount of thorium dioxide injected in most of the reported animal experiments has been several times larger than that used in man. Moreover, the susceptibility of other species to the induction of tumors may not be comparable to human susceptibility. Therefore, all that can be stated on the basis of animal experiments, and a review of the questionnaire to follow, is that, despite the paucity of authentic thorotrast-induced tumors in man, the results of animal experimentation appear to justify the conclusion that the potential hazard of carcinogenicity must be considered and may perhaps be verified

TABLE I: OBSERVATIONS IN 20 CASES COMING TO AUTOPSY AFTER ADMINISTRATION OF COLLOIDAL THORIUM DIOXIDE

Interval Between Administration of Thorotrast and Death	No. of Cases	Autopsy Findings
1 month or less	13	Polymorphonuclear or lymphocyte infiltration of liver, vacuolization and multiple small areas of necrosis and Kupffer cells loaded with thorotrast
2 to 3 months	3	Areas of necrosis of liver cells with lymphocyte infiltration, vacuolization of liver cells and widening of intercellular spaces. Kupffer cells loaded with thorotrast
15 months	1	Mild fibrosis in liver. Thorotrast in clumps of Kupffer cells
5 years	1	Fibrosis of liver giving an appearance of cirrhosis. Fibrosis marked in hilar lymph nodes of liver (see Fig. 1). Moderate fibrosis in spleen. Scattered areas of necrosis in liver with thorotrast largely extracellular, particularly in areas of fibrosis
6 years	1	Fibrosis of liver with isolation of lobules by fibrous tissue. Scattered areas of nodules of fibrosis with giant cells. Liver hilar lymph nodes replaced by fibrous tissue
7 years	1	Fibrosis of liver with isolation of lobules. Multiple islands of fibrous tissue with heavy deposits of thorotrast, largely extracellular. Lobular architecture destroyed

in the future. It was on this basis that the Council on Pharmacy and Therapeutics of the American Medical Association in 1932 withheld its approval of thorium dioxide for clinical use (18).

B. Fibrosis: Late fibrosis at the site of accidental subcutaneous or perivascular injection and cirrhosis at the site of liver deposition have been reported sporadically but not generally recognized as frequent complications of thorotrast injection (40, 49, 69; see Table I). Pohle and Ritchie (63) studied the changes in rabbits after the injection of thorium and separated the pathological findings into three stages: vacuolization of the liver cells and endothelial swelling, followed by fatty degeneration and acute necrosis of the liver, and late fibrosis (see Fig. 2).

Jacobson and Rosenbaum, reporting the postmortem findings in a case examined five years after injection of thorotrast, described retraction of liver lobules with microscopic deposition of thorium dioxide particles in the periportal spaces and lying free in the extracellular spaces, some increase in fibrous tissue, and a moderate amount of degeneration of liver cells (40). There was, however, marked fibrosis of the lymph nodes at the hilus of the liver. These writers estimated that 27 per cent of the originally injected 75 c.c. of thorotrast was still present in the liver, as determined by measurements of radioactivity.

Amory and Bunch have presented thorough descriptions of extreme degrees of fibrosis as a result of accidental extravascular injection of thorotrast (1).

Even a cursory survey of existing pathological material both in the literature and in our own studies reveals numerous other instances in which migration of the particles to the hepatic hilar lymph nodes and other structures (see Fig. 7) has occurred, with massive deposition, progressive fibrosis, and eventual complete obliteration of the architecture (see Fig. 1).

The migration and aggregation of thorotrast have been worked out experimentally by Wilson, whose studies tend to corroborate the roentgenographic observation of delayed opacification of hepatic hilar lymph nodes (86–88). Another very detailed report by Schmidt, Schulte, and Lapp further confirms this (69).

Other evidence of migration is to be seen in the change of the density of the liver and spleen from a completely uniform opacity to a markedly reticular pattern (see Figs. 3, 4 and 5). It is adjacent to the periportal areas that the parenchymal fibrosis takes place. Jakob and Wachsmann have emphasized that this fibrosis may be enhanced at the interface between collections of thorium dioxide (or any diagnostic medium) and tissue after exposure to diagnostic or therapeutic irradiation (41). This needs additional study.

Further evidence of late fibrosis may be found in a case of endothelial-cell sarcoma of the liver reported by MacMahon *et al.* (49). The tumor-free areas of the liver revealed, on the one hand, almost normal zones containing little or no microscopic thorium dioxide and, on the other hand, areas of heavy deposition with loss of all structural detail; fibrotic scars replaced the liver cells particularly about the central veins. An increase in collagen deposition was noted in the portal areas, with obliteration of the lymphatics.

A review of the experience with thorium dioxide in colloidal suspension at Stanford University Hospitals yielded a series of 20 autopsy cases in which death occurred at varying intervals after administration of the opaque material (see Table I). Four of the patients survived more than one year following injection, and in all of these the liver exhibited some degree of fibrosis. In 3 the fibrosis was extensive, but in 1 of that number there were other factors which might well have accounted for the fibrosis in the absence of thorium dioxide deposition.

Finally, experimental evidence exists that fibrosis develops at the sites of deposition of colloidal thorium dioxide after injection in animals (2, 6, 7, 37, 59, 75, 76, 80).

It is not clear whether the fibrosis re-

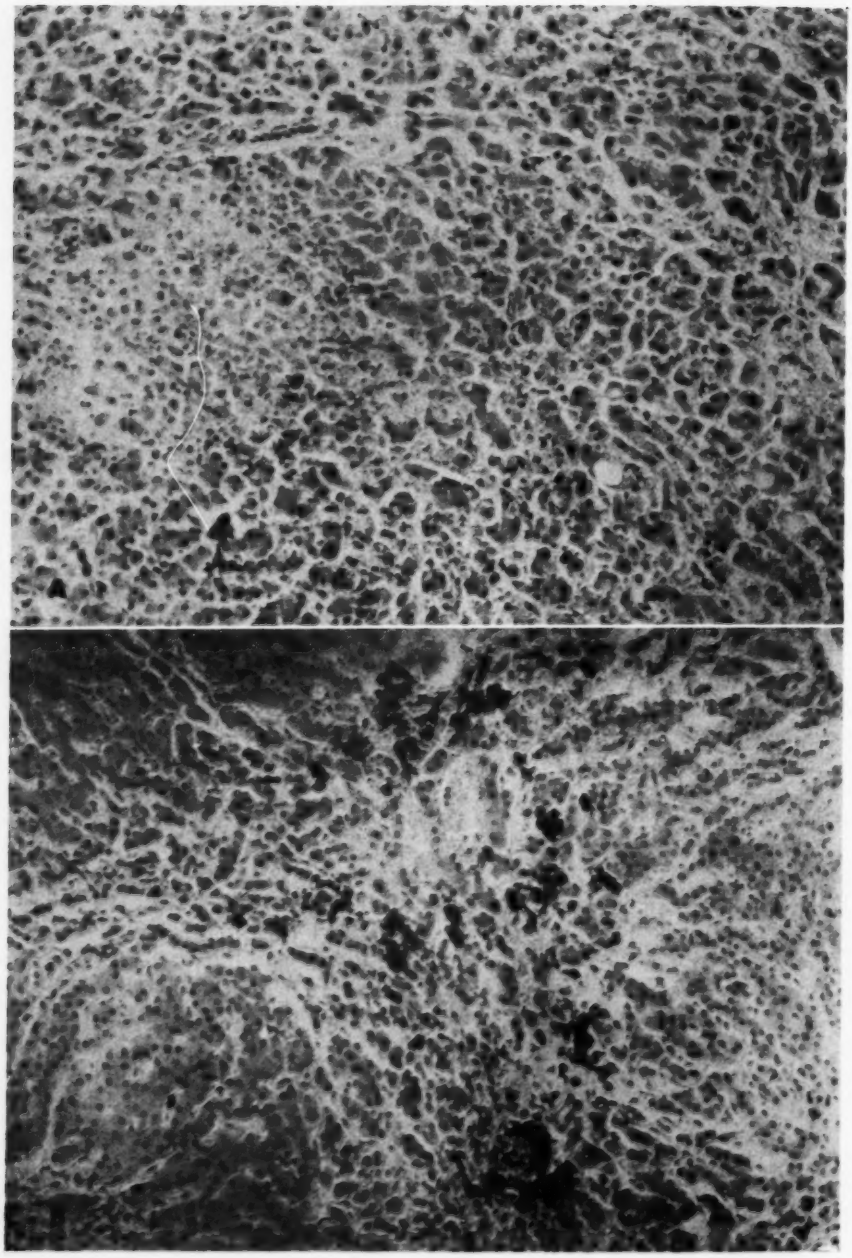


Fig. 2. Pathological changes in the human liver following administration of thorotrast. A. Early: Part of the cells already show some vacuolization and there is disturbance of some of the normal architecture. B. Later: Edema with dilated lymphatics and increased fibrous tissue. There are also perivascular aggregation of granules of thorotrast and disruption of the normal architecture. For still later changes, see Fig. 2, C.

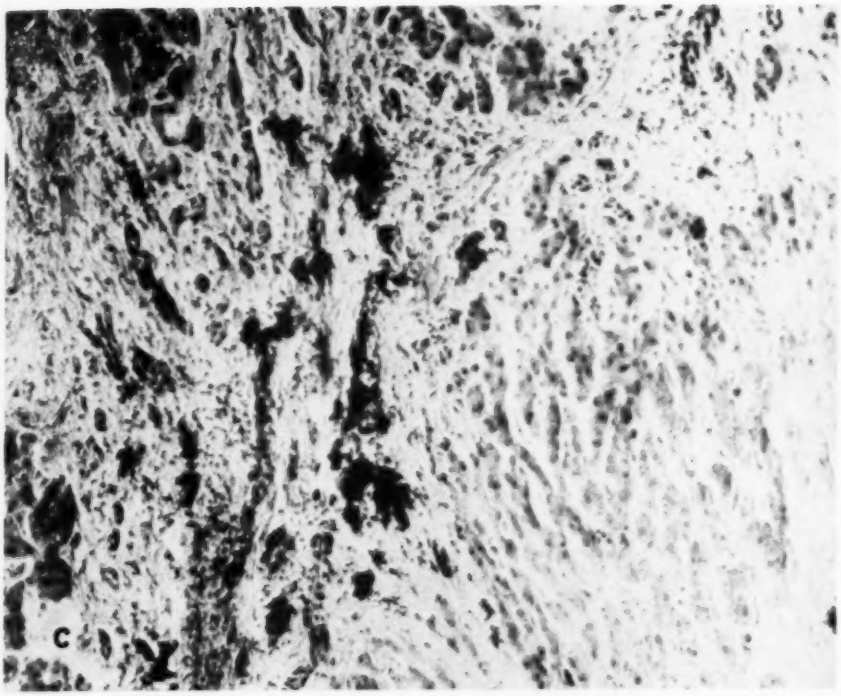


Fig. 2, C. Late changes in the liver following administration of thorotrast. Marked fibrosis with atrophy and obliteration of the architecture.

sulting from thorium dioxide deposition is the result of local alpha irradiation, gamma irradiation, or a chemical reaction to thorium like that which occurs after the deposition of silicates in the lung. The effect is probably not the non-specific result of the accumulation of particulate matter in macrophages, since aggregates of india ink or iron oxides do not produce fibrotic changes (14, 29, 33, 42). Since thorium dioxide is rather highly insoluble and is a known source of significant local radiation, it seems more reasonable to conclude that the changes are due to radiation and not to direct chemical action.

Thus it would appear that late degenerative changes, of which fibrosis is the most striking, are not at all uncommon after the injection of colloidal thorium dioxide. These fibrotic changes may be disabling when they occur in extravascular or extravisceral injection sites and may well be of clinical significance when widely distributed in the liver in patients who survive sufficiently long after thorotrast injection.

Since the use of thorotrast has fallen into disfavor largely on the basis of isolated case reports, an attempt has been made to obtain a larger amount of information by distributing a brief questionnaire to 167 radiologists, inquiring as to their use of thorium dioxide, its side effects, and possible production of malignant neoplasms. Stress was laid on the length of time that the thorium dioxide remained in the tissues. Replies were obtained from 132 radiologists. Of these, 64 reported that they did not use thorium dioxide and 13 spontaneously expressed disapproval of its use. A total of some 4,325 cases were reported by 68 radiologists. In approximately half of this number the medium was used for hepatolienography; mammography, angiography, pyelography, examination of sinus tracts, and cholangiography accounted for 507 cases. In the remainder,

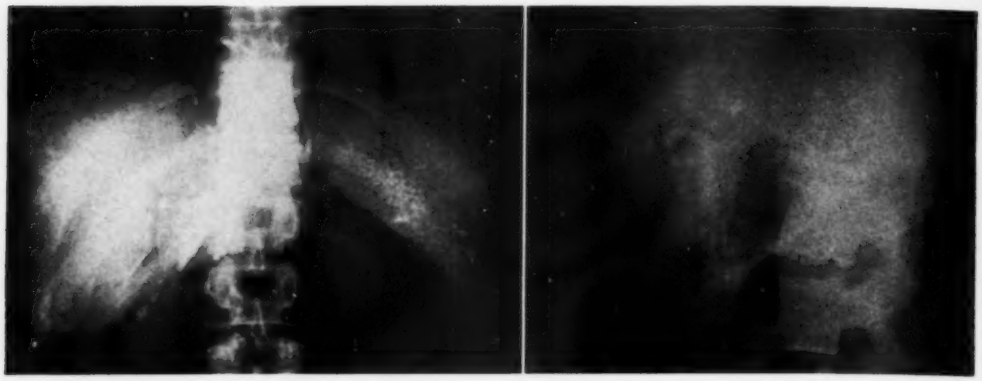


Fig. 3. Anteroposterior and lateral roentgenograms of the upper abdomen of a patient given 75 c.c. of thorotrast nine years before, in whom a biliary duct carcinoma developed. Note the reticular pattern of the thorotrast in the spleen; also, the densities adjacent to the hilar region of the liver, close to the site at which the carcinoma was biopsied. The opacity of the liver has a mottled irregular character further illustrating the migration and aggregation of thorotrast. This case was sent to us by Dr. R. A. Carter, from the Los Angeles General Hospital.

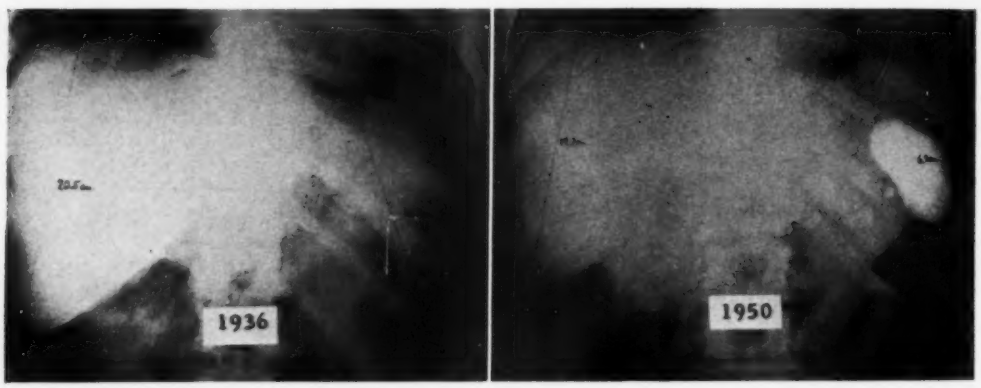
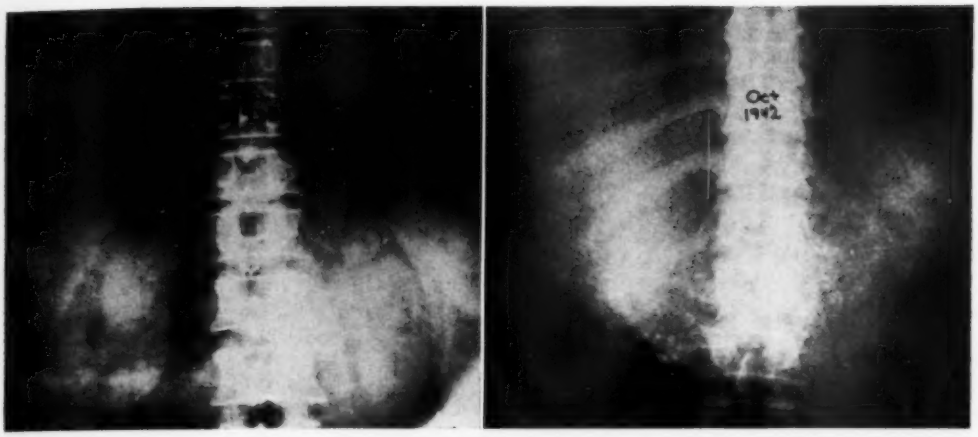


Fig. 4. Change in the size of the spleen from 13.7 cm. in 1936 to 6.9 cm. in 1950, with a mottled appearance in the latter year which was not seen originally. Note the migration of the thorotrast to lymph nodes adjacent to the spleen. Other lymph nodes, in the hilus of the liver, also contain opaque material but the shadows are poorly reproduced. The shadow of the liver has shrunk but little; however, the density has changed from uniform to reticular (again not well reproduced). Liver biopsy showed increase in fibrous tissue in periportal regions.

about 2,000, the type of examination was unspecified.

The greatest value of the questionnaire appeared in some of the comments made in the discussion of individual cases. Whereever the questionnaire elicited the fact that thorotrast had been used, a follow-up letter was sent to inquire as to details, if they had not been given previously. These letters gave some idea of the incidence of fibrosis, especially in the perivascular structures; almost one-fourth of those reporting mentioned it. The cases of malignant lesions appearing in the literature were brought to our attention in replies both to the questionnaires and to our letters. To our surprise, only two such unpublished cases not already known to us thus came to light.

In summary, it seems reasonable to conclude that the induction of malignant neoplasms as a result of local radiation injury at the site of deposition of thorium dioxide is a potential rather than an important clinical hazard. The instances of hepatic malignant neoplasms in patients



who have received thorium dioxide are too few to be significant, and the questionnaire gave no support to the view that this is as yet an important complication of the use of this medium.

A much more serious problem is the late fibrosis and scar formation which may occur either in the liver and spleen or in sites of accidental extravascular injection. It is our impression that this complication has been insufficiently emphasized and that it occurs with sufficient frequency to constitute a justifiable contraindication to the further use of thorium dioxide for hepatolienography and other diagnostic procedures except in extreme urgency or where life expectancy is thought to be very short.

Fig. 5. Film made in 1938 shows a large space-occupying lesion of the right lobe of the liver which in 1942 had grown still larger. Note the change in the character of the density below the lesion and the accumulation of the thorotrast in the lymph nodes of the hilus of the liver. The patient, a 72-year-old Greek, died, and the reticular pattern of the material can be seen in the reproduction of the roentgenogram of the liver. The diagnosis was echinococcus cyst.

II. CHARACTERISTICS OF AN IDEAL MEDIUM

There remains a need for the diagnostic opacification of the liver and spleen (and placenta) in a variety of clinical conditions. It seems desirable to profit by our long experience with colloidal thorium dioxide and to formulate the characteristics of an ideal opaque medium for hepatolienography. Such an ideal medium (*a*) should have little or no acute or chronic toxicity; (*b*) should not be radioactive; (*c*) should be of sufficiently high atomic number to afford good opacification without administration in excessive amounts; (*d*) should be administered easily, preferably orally but intravenously if necessary; (*e*) should have a high affinity for selective deposition in the liver and spleen; (*f*) if possible, should be safely and rapidly eliminated from the body. It seems unlikely that a single medium fulfilling all of these criteria can be obtained.

III. EXPERIMENTAL STUDIES WITH NEW MEDIA

In recent years a few materials have been brought forth, of which the most promising have been the ethyl ester of the tri-iodide

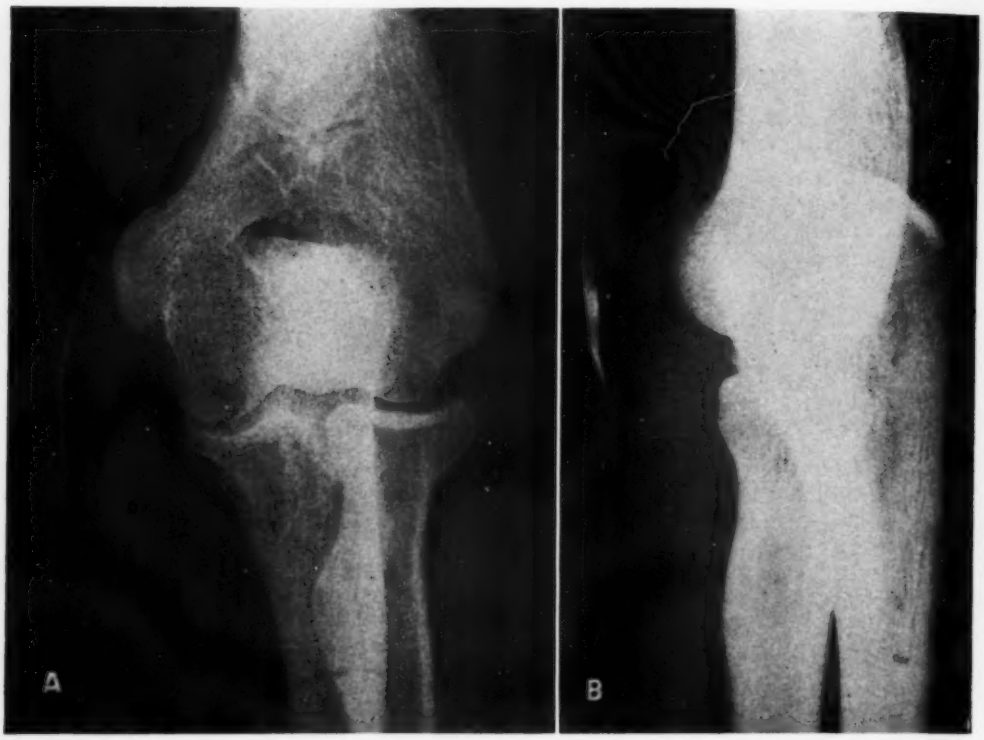


Fig. 6. Hard plaque-like deposits palpable in the soft tissues of the antecubital fossa following the injection of thorotrast. A. Five years after injection. B. Another case, four weeks after injection.

of stearic acid ("Jodsol") and other halogenated fatty acids (4, 5, 13, 36, 61). The former has produced occasional acute toxic reactions and therefore cannot be considered as an entirely satisfactory medium (61). The brominated fatty acids developed by Olsson represent a step forward in that they are orally administered and produce adequate opacification of the liver and spleen in rats, following which the material is rather rapidly eliminated (62). However, these compounds suffer from the disadvantage that massive quantities of bromine or iodine are required for satisfactory opacification. It is likely that a significant number of individuals will be sensitive to iodine and bromine and that the large amounts involved may be expected in many instances to yield allergic or toxic reactions.

Attempts have been made to use iodized oils suitably emulsified or homogenized; these have the advantage that they can be eliminated from the body after administration but again suffer from the inherent disadvantage that a large amount of material must be given to achieve satisfactory opacification. Moreover, controlling the particle size of the oil droplets is of critical importance in the elimination of acute embolic phenomena and ensuing severe or fatal reactions during intravenous administration.

One field which has not been explored extensively is placentography. The placenta has a rich supply of reticulo-endothelial elements. Obviously materials which are radioactive are not feasible for use here. It is easy to foresee that if an emulsion could be made practically nontoxic it would be most useful in placentography (9, 19, 20, 21, 36, 43, 56, 82).

Another line of approach is the development of colloidal suspensions of highly in-

Fig. 7. Case from Dr. E. L. Pirkey, Louisville, Ky., showing the outline of the gallbladder wall due to accumulated thorotrast. (See Pirkey *et al.*: Am. J. Roentgenol 66: 208, 1951, especially the radioautographs.)

soluble heavy inorganic materials similar in principle to colloidal thorium dioxide but utilizing elements of slightly lower atomic number which are non-radioactive and non-toxic. Such materials are given intravenously and taken up by the reticulo-endothelial cells. If the particle size is suitably adjusted, selective deposition in the liver and spleen can be anticipated (33). The inherent disadvantage of this type of material is that it tends to remain in the body for long periods of time and may never be eliminated. The possibility of late fibrosis again arises, although non-radioactive inorganic materials other than the silicates usually do not produce significant local fibrotic reactions (14, 29, 33, 42). On the other hand, Fleming and Chase state that in the case of thorotrast in subcutaneous tissues "the metallic irritation produces fibroblastic proliferation and hyaline fibrosis" (25).

Inorganic Metallic Compounds: Tantalum has been selected by one of us (G. W. H.) as a promising metal to replace thorium as an agent for uptake by the reticulo-endothelial system. It is almost inert, has no known toxicity (10, 17, 60), and is not radioactive. Experimental investigations have been undertaken with compounds of tantalum in a colloidal state. Initially, tantalum pentoxide was dissolved in a strongly alkaline solution which was subsequently dialyzed to neutrality to yield clear colloidal suspensions. The concentration of these suspensions was found to be too low. More recently, concentrated hydrosols of tantalum pentoxide with very satisfactory levels of radiopacity have been studied.[3] These suspensions have been non-toxic over long periods of

[3] These hydrosols have kindly been supplied for us through Dr. Charles Mann of the Heyden Chemical Corporation, New York, N. Y.

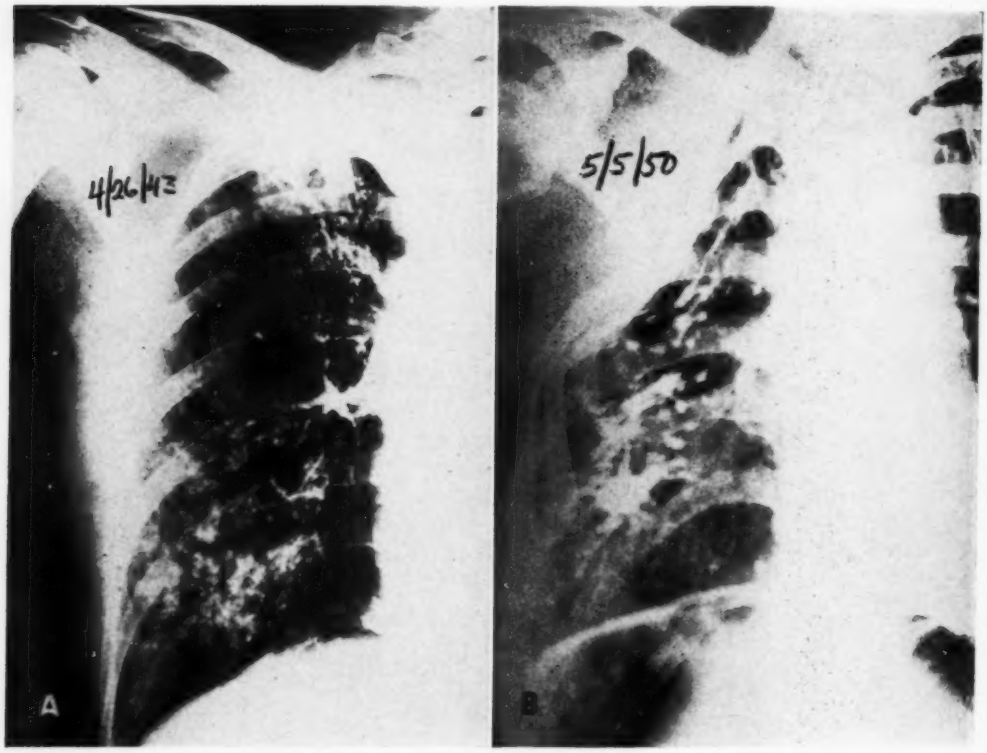


Fig. 8. A. Bronchogram made with thorotrast in 1943 because the patient was sensitive to iodine. B. Seven years later after a two stage thoracoplasty. Note the aggregation of opaque material.
The patient is alive and well, with a negative sputum at present. This procedure is not recommended.

time after subcutaneous, intramuscular, or intraperitoneal injection into mice. The injected material appears to have a level of radiopacity which may be clinically useful (see Fig. 9). Intravenous injection of significant amounts of this preparation into mice has led to fatal reactions which appear to be embolic in nature. The pentoxide of tantalum is known to be thixotropic, and ampules of the experimental hydrosol have, upon standing, formed solid gels which could be liquefied after forceful agitation. It seems likely, therefore, that gel particles present in apparent liquid suspensions of this type may lead to emboli. Microscopic sections of lungs of mice which have suffered fatal reactions after intravenous injection reveal obstruction of the finer arterial vessels of the lung by conglomerated masses of particles.

For this reason, attention is now being directed to colloids prepared directly from powdered metallic tantalum. Although much work remains to be done, the radiopacity and lack of general toxicity of these preparations have been encouraging and it is hoped that safe colloidal preparations will soon become available.

Iodized Oil Emulsions: About four years ago one of us (H. S. K.)[4] prepared a series of emulsions of iodized poppy-seed oil (lipiodol) in blood serum, using a needle valve homogenizer to disperse the oil droplets. Thick creamy emulsions were obtained, from which the largest particles began to settle out in a few minutes, leading to the formation of an oil layer at the bottom. The remaining emulsions proved to be relatively stable for several hours.

[4] This work was carried out in the Department of Radiology, Yale University School of Medicine, under the supervision of Dr. Hugh M. Wilson.

The emulsified material was injected into mice, guinea-pigs, and rabbits. In a few instances moderately good opacification of the liver and spleen was noted. Uptake of opaque material was optimal in the liver an hour and a half after injection, with a shift to the spleen in two and a half to three hours. In several instances, however, significant fluctuations in particle size in the emulsion led to sudden death during or shortly after injection of the material, presumably due to emboli.

In 1942, Dr. R. R. Newell suggested locally that attempts at hepatolienography be made with emulsions of radiopaque oils, a suggestion which has been discussed elsewhere (28). One of us (S. F. T.) for some time thereafter made emulsions according to the method of Holt *et al.* (39) without the knowledge that other similar investigations had been carried out abroad. Degkwitz (13) and Beckermann (4, 5) studied the properties of the tri-iodide of the ethyl ester of stearic acid in colloidal suspensions ("Jodsol"). While their early results were promising, the material was found to be unsatisfactory for clinical use because it is readily metabolized, releasing a great deal of iodine, which is a disadvantage of all of the compounds of this type. The metabolic breakdown of over 15 gm. of iodine (61), the amount necessary to produce opacification of the liver and spleen in an adult, is to be considered. Recently Olsson has used brominated emulsified sesame-seed oil orally with good opacification of the liver and spleen of rats, but no reports of the use of this material in man have yet appeared (62). There is no reason to believe that the even larger amounts of bromine necessary for opacification can be metabolized any more safely than iodine. In a series of experiments, one of us (S. F. T.) prepared emulsions of iodinated oils and injected these into rabbits. Satisfactory opacification of the liver and spleen was obtained (see Fig. 10), but embolic phenomena occurred in some instances, indicating the potential hazards of the use of this material.

The use of new types of wetting agents and perhaps the addition of protective colloids may lead to the development of tougher, more homogeneous emulsions which will be stable enough to remain in suspension for considerable periods of time, will withstand autoclaving, and will be of sufficient small and uniform particle size to be administered intravenously with safety. If such preparations could be developed, they would have the advantage over metallic inorganic compounds of being excreted from the body after their diagnostic function had been fulfilled.

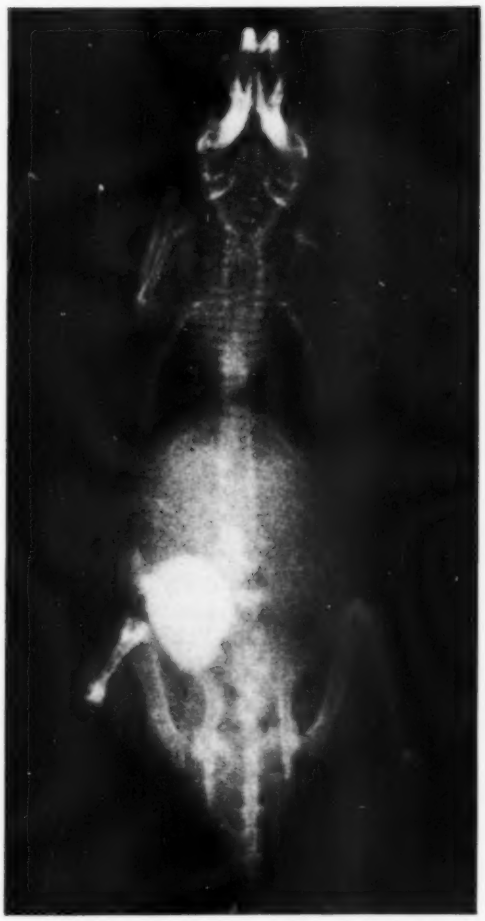


Fig. 9. Roentgenogram of a mouse which had been injected with 0.5 c.c. of a 10 per cent hydrosol of tantalum, found between the leaves of the mesentery. Note that the sharp outline and density are quite satisfactory.

Recent studies in complete parenteral

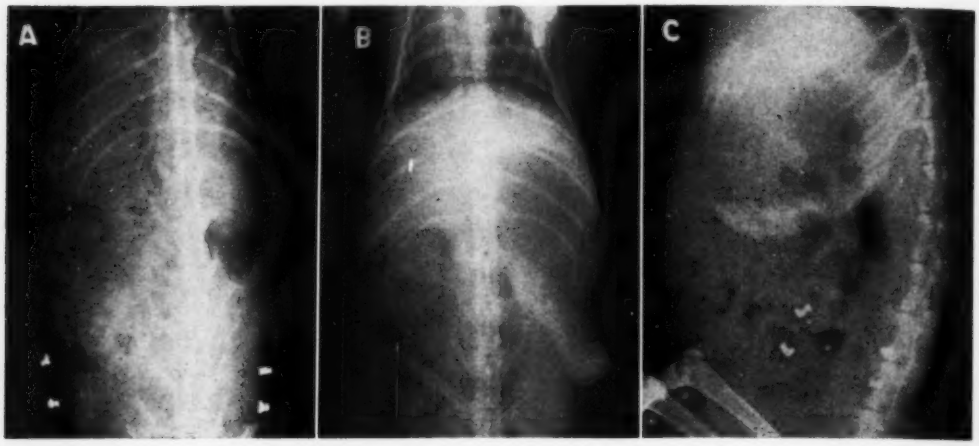


Fig. 10. Opacification of the liver and spleen of a rabbit with a 10 per cent emulsion of iodized peanut oil (iodochloral). Satisfactory density of the liver and spleen are clearly demonstrated. A. Preliminary film. B and C. Two views three and a half hours after injection of between 5 and 6 c.c. of emulsion. Done in 1942

alimentation of patients (and animals) has brought out some technics in the preparation of emulsions which have not been completely explored (11, 30, 31, 32, 35, 48, 53, 54, 55, 71). In the past few weeks, highly improved emulsions of both iodized poppyseed oil (lipiodol) and iodized peanut oil (iodochloral) stabilized with a new wetting agent[4] have been prepared for us by Dr. William Talbot. Toxicity tests and determinations of droplet size have not yet been completed, but preliminary observations indicate that droplet size is smaller and considerably more uniform than in emulsions we have previously prepared. Moreover, the new emulsions are highly stable and do not separate visibly after standing for periods up to six weeks. Injection of these emulsions intravenously into mice has been followed by no untoward sequelae to date. Within ten minutes after injection excellent opacification of the spleen and slight opacification of the liver have been demonstrated (see Fig. 11). Although insufficient data are available at this time, it is our impression that opacification becomes maximal at thirty to sixty minutes after injection, remains essentially unchanged during the first twenty-four hours, and slowly diminishes during the next few days. Further experimental work with these emulsions is in progress.

[4] Amine ES, Union Carbide and Carbon Corporation.

SUMMARY

The possible injurious effects of colloidal thorium dioxide (thorotrast) as a contrast medium for hepatolienography are considered on the basis of a review of the literature and 132 replies to a questionnaire addressed to 167 radiologists. Only 5 instances of malignant growth following the injection of thorotrast were found. In view of the long standing and widespread use of the medium, this is not held to indicate a carcinogenic effect in man.

A much more serious problem is the late fibrosis and scar formation which may occur either in the liver and spleen or in sites of accidental extravascular injection. It is believed that this complication occurs with sufficient frequency to constitute a justifiable contraindication to the use of thorium dioxide for hepatolienography or other diagnostic procedures except in cases of extreme urgency or where life expectancy is short.

The use of the ethyl ester of the triiodide of stearic acid ("Jodsol") and of the brominated fatty acids for demonstration of the liver and spleen, as reported in the German and Swedish literature, is cited.

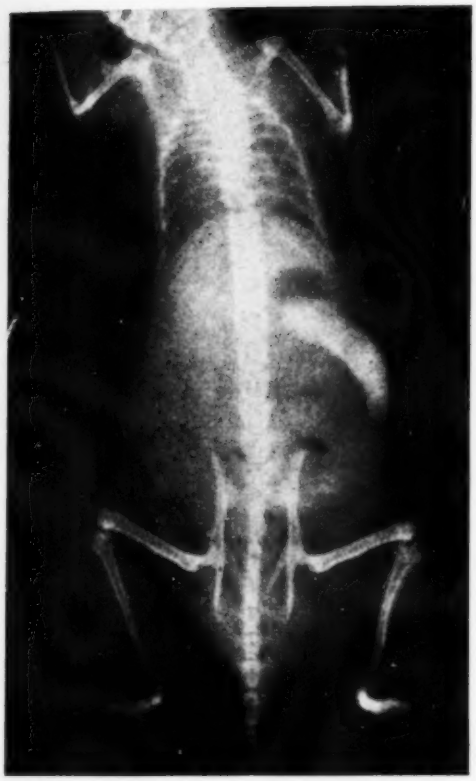


Fig. 11. Study made in November 1950, showing slight opacification of the liver but excellent opacification of the spleen of a mouse one and a half hours after injection of 0.3 c.c. of a 25 per cent emulsion of iodized poppy-seed oil (lipiodol). Film made three hours after injection. The shadow of the spleen was diminished at twenty-eight hours and gone at three days.

Original experimental studies of possible new media for hepatolienography are reported, including (1) inorganic metallic compounds such as tantalum and (2) iodized oil emulsions, stabilized with new types of wetting agents. Work along these lines is still in progress.

ACKNOWLEDGMENT: Dr. George Barnett has been most helpful in translating the foreign literature. Drs. E. R. Miller and C. E. Duisenberg assisted in the preparation of many of the early iodized oil emulsions. Dr. William Talbot made the most recent emulsions, using the facilities of the Palo Alto Medical Research Foundation.

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SUMARIO

La Hepatolienografía: Pasado, Presente y Porvenir

Tomando por base un repaso de la literatura y 132 contestaciones a un cuestionario dirigido a 167 radiólogos, considéranse aquí los posibles efectos nocivos del bióxido de torio coloidal (torotrasto) como medio de contraste para la hepatolienografía. No se encontraron más que 5 casos de tumor maligno consecutivo a la inyección de torotrasto, y en vista del largo y generalizado empleo del medio, no se cree que esto indique efecto carcinógeno en el hombre.

Un problema mucho más grave es planteado por la tardía fibrosis y formación de cicatrices que puede ocurrir en el hígado y el bazo o en sitios de fortuita inyección extravascular. Parece que esta complicación sobreviene con suficiente frecuencia

para constituir una contraindicación justificada del uso del bióxido de torio para la hepatolienografía u otros procedimientos de diagnóstico, salvo en casos de urgencia extremada o cuando es breve la expectativa de vida.

Cítase el uso del éster etílico del triyoduro del ácido esteárico (jodsol) y de los ácidos grasos bromados para la observación del hígado y el bazo, según lo describe la literatura alemana y sueca.

Preséntanse estudios experimentales originales de nuevos medios posibles para la hepatolienografía, comprendiendo: (1) compuestos metálicos inorgánicos, tales como el tantalio y (2) emulsiones de aceite yodado, estabilizadas con nuevas formas de humectantes.

Roentgen Demonstration of the Venous Circulation in the Liver: Portal Venography[1]

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VASOGRAPHY has proved to be one of the most fruitful fields of roentgen investigation in recent years. With the hope of further extending its scope, a study of the roentgen demonstration of the portal circulation of the liver has been instituted at the University of Minnesota. This demonstration has been given the descriptive designation portal venography.

possible under certain specialized circumstances, such as a pre-existing portacaval anastomosis or portal obstruction with secondary dilatation of the periumbilical veins. The great majority of cases, however, require an internal approach which necessitates laparotomy.

Using an external approach, Fariñas obtained good contrast filling of the portal

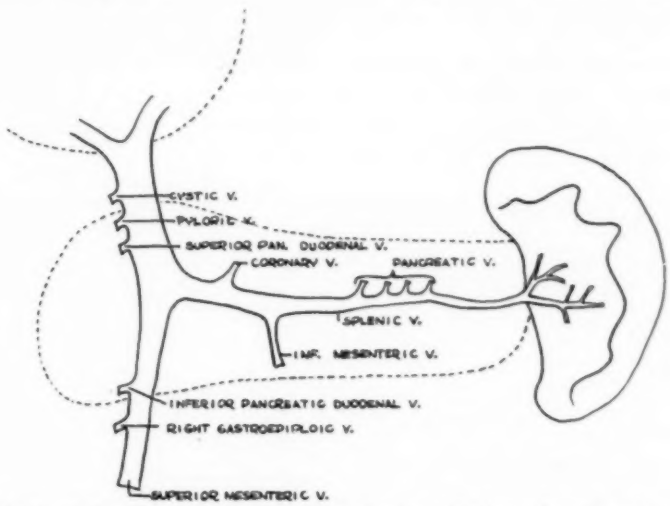

Fig. 1. The extrahepatic portal system of veins. (Redrawn from Douglass and Baggenstoss.)

The literature contains several references to portal venography, but these are concerned for the most part with the extrahepatic portal system. Little interest has been evidenced in the intrahepatic portal circulation, which is the subject of this paper.

Due to its relative inaccessibility, the various methods of approach to the portal circulation present difficulties from a diagnostic standpoint. An external approach is

vein and the portal radicles within the liver by means of contrast material injected into the long saphenous vein in cases where a portacaval anastomosis was present. More recently Dotter and his co-workers were able to pass a catheter directly into the portal vein through a portacaval anastomosis. This external approach resulted in a visualization of the portal radicles similar to that obtained by Fariñas. In the presence of portal ob-

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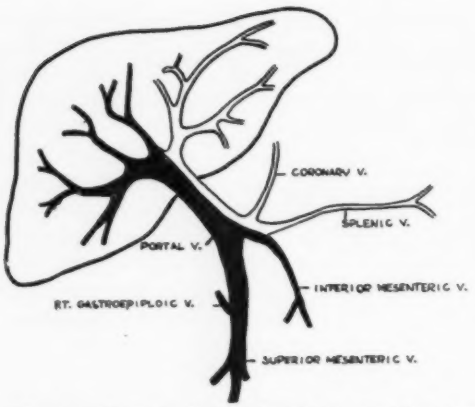

Fig. 2. Diagram of the channels of streamline flow in the portal vein. The blood from the mesenteric veins (black) is directed to the right side of the liver. The blood from the spleen (white) is directed to the left.

struction with concomitant dilatation of the periumbilical veins, Celis and his associates visualized the portal circulation by means of contrast material injected into these dilated veins.

Blakemore and Lord have used an internal approach to portal venography at operation to demonstrate the site of extrahepatic portal obstruction. Child *et al.* have also used operative portal venography in their studies of the effects of complete occlusion of the portal vein and have satisfactorily demonstrated the extrahepatic portal system.

In evaluating the problems of portal venography precise information concerning the anatomy and dynamics of the portal circulation is desirable. On the basis of the study of 92 autopsy cases Douglass, Baggenstoss and Hollinshead present a diagram of the most constant configuration of the extrahepatic portal system (Fig. 1). The work of these authors probably represents the most reliable data on this subject available at the present time, since the diagrams of the portal system found in most standard texts and atlases of anatomy were made from a single dissection.

The intrahepatic circulation is well described by McIndoe in his paper on the vascular lesions of portal cirrhosis. McIndoe prepared for study a number of corrosion specimens of the vascular tree in both normal and cirrhotic livers. According to him, the portal vein consists of a massive system of branches ascending directly without cross anastomoses through five or six successive orders of division into the sinusoidal circulation. In general, the branches are given off at right angles to the parent stem, while the sinusoids arise from the tips of the venules. The hepatic artery lies in close relationship to the portal vein and often winds around it. The relationship of the portal and hepatic veins is that of two huge venous systems dovetailing into each other so regularly and exactly that no two vessels come in contact and all terminals are at the greatest possible distance from one another. The intervening space is occupied by hepatic cells. McIndoe found that this precise arrangement of the vascular channels is grossly distorted in cirrhosis.

From time to time there have appeared in the literature data suggesting that the blood entering the liver from the portal circulation does so in more or less discrete channels of streamline flow. For example, blood from the spleen is thought to be diverted largely to the left side of the liver, while that of the mesenteric veins tends to move to the right (Fig. 2). This concept is of considerable interest with regard to metastatic involvement of hepatic tissue from primary tumors in the mesenteric areas. Also, this concept probably has some bearing on the distribution of contrast material in the liver in portal venography.

Following preliminary animal and autopsy studies, portal venographic examinations were performed at the University of Minnesota Hospitals as an incidental procedure during various surgical operations requiring laparotomy. The first step in the technic used is the insertion of a polythene catheter into one of the tributaries of the portal vein. The right gastroepiploic vein has most often been used. After insertion, the catheter is advanced proximally into the portal vein and is tied in place. Twenty cubic centimeters of 35

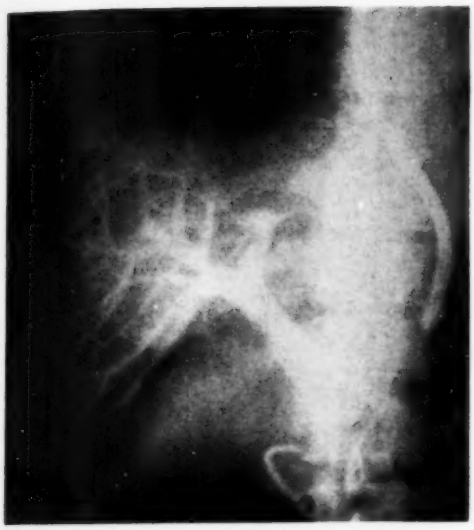

Fig. 3. Good filling on the right with only partial filling on the left. Note polythene catheter in place at junction of right gastro-epiploic vein and portal vein.

per cent diodrast are then injected through the catheter as rapidly as possible. Preferably the injection should be completed in two or three seconds. Immediately upon completion of the injection a radiographic exposure is made. For this a mobile 50-ma. x-ray machine and a hand-operated Potter-Bucky diaphragm have been used.

With the technic described, satisfactory portal venograms have been obtained with reasonable consistency. Good contrast filling of the portal radicles of the right lobe of the liver is, as a rule, more constant than filling of both lobes (Fig. 3). Filling of the portal radicles of the left lobe with poor filling of the right lobe of the liver has not been observed. These observations may well be due to the previously stated concept of streamline flow in the portal vein.

In most of the portal venographic ex-

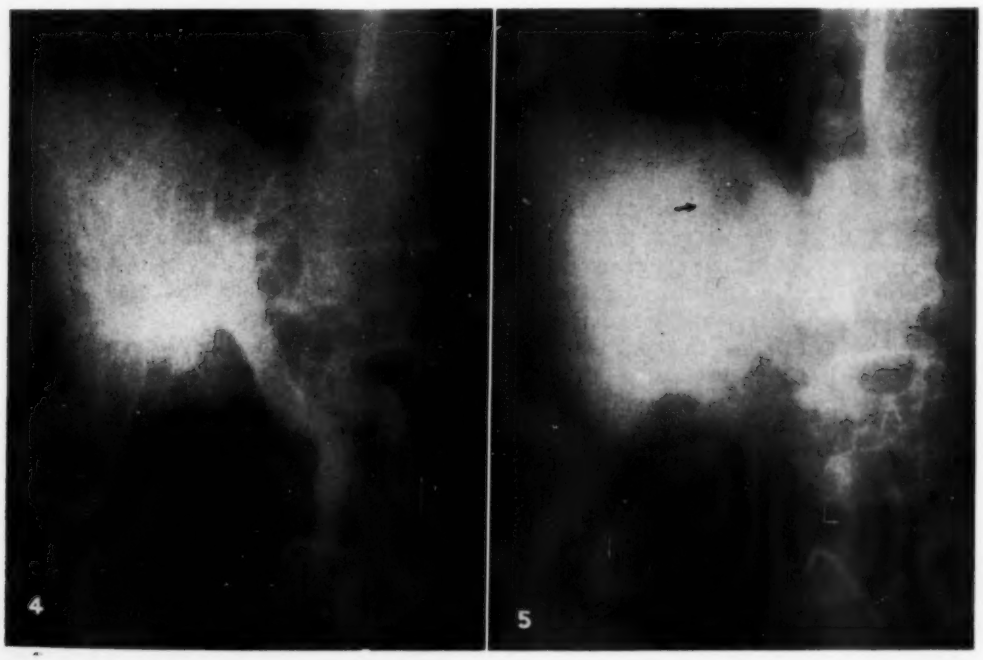

Fig. 4. Portal venography with 70 per cent diodrast. Patient had carcinoma of the rectum with multiple abdominal metastases. Note indentation of main portal trunk by an enlarged lymph node.

Fig. 5. Same case as Fig. 4. Delayed exposure with 70 per cent diodrast. The contrast material has reached the sinusoidal circulation, producing a generalized increase in the density of the liver. A large metastatic focus can be identified as an area of decreased density in the liver.

Figures 4 and 5 were not included in the original reading of the paper but were added at a later date.

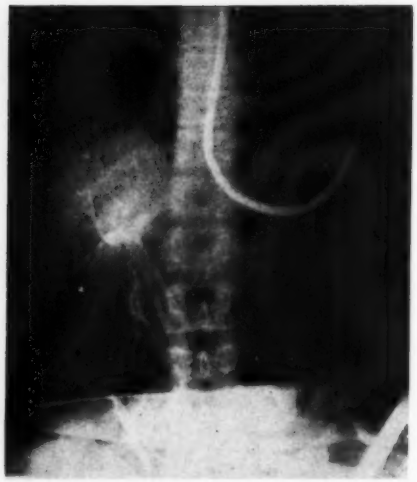

Fig. 6. Retrograde flow of contrast material into portal tributaries. Both the coronary vein and the veins draining the gallbladder region can be identified.

aminations, 35 per cent diodrast has been employed, although several examinations have been performed with 70 per cent diodrast (Fig. 4). While better contrast can be expected with the more concentrated solution, it has not been used routinely because of the possibility of serious reactions. Opacification of the liver as a whole may, however, be desirable, and such opacification necessitates the use of 70 per cent diodrast. With the 70 per cent preparation, temporary opacification comparable to that obtained with thorotrast can be accomplished by delaying the radiographic exposure so as to allow the contrast material to reach the sinusoids of the liver (Fig. 5). This type of visualization requires more precise timing than visualization of the portal radicles. The use of a rapid cassette changer to permit multiple serial radiographs would eliminate, to a great extent, the difficulties in timing of the exposure. However, no practical equipment of this type that can be adapted to the operating room is at present available.

Most of the unsatisfactory examinations were the result of failure to pass the tip of the catheter into the main portal trunk, or of failure to inject the contrast material into the circulation with sufficient rapidity. In the former instance, the contrast material was often dissipated into the tributary portal channels (Fig. 6). When the contrast material was not injected with sufficient rapidity, its excessive dilution in the blood stream resulted in faint visualization or none at all. The contrast material, when properly injected, appears to move along as a unit, and this favors optimum concentration of the medium in the venous radicles (Fig. 7).

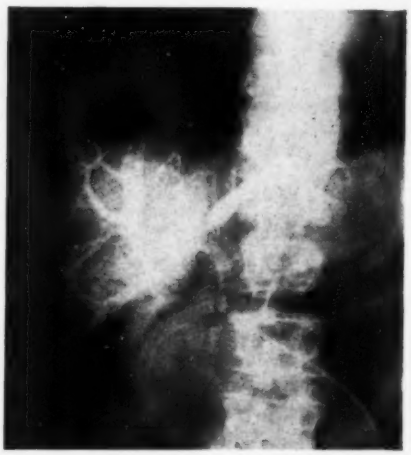

Fig. 7. Sharp demarcation between densely filled portal radicles and main portal trunk. The contrast material appears to move along as a unit.

There have been no serious reactions or complications resulting from portal venography. In one instance a decrease of 30 mm. in the systolic blood pressure occurred shortly after the injection. This phenomenon was transitory. On two occasions there was extravasation of the contrast material (Fig. 8). This complication may be attributed to excessive stress of the rapid injection when the tip of the catheter lies in a relatively small portal tributary. Again, it is emphasized that the tip of the catheter must be advanced into the main portal trunk. No sequelae of consequence resulted in the cases in which extravasation occurred. Furthermore, films taken one hour after the injections revealed that almost complete absorption had taken place.

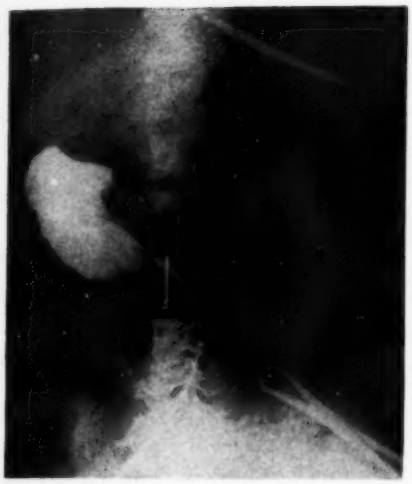

Fig. 8. Extravasation of 70 per cent diodrast from a small mesenteric vein into the surrounding tissues.

The experience gained in this investigation tends to indicate that portal venography is a technically feasible procedure and that it is relatively safe. Its practical applications await the determination of the alterations from the normal that may be recognized in the presence of pathological changes in the liver.

CONCLUSIONS

1. Portal venography is a technically feasible and relatively safe procedure.

2. Portal venography tends to substantiate the concept of streamline flow in the portal vein.

3. Further experience in pathological conditions of the liver may prove the practicality of portal venography as a diagnostic procedure.

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SUMARIO

Observación Roentgenológica de la Circulación Venosa en el Hígado: La Venografía Porta

En los Hospitales de la Universidad de Minnesota, han llevado a cabo, como procedimiento incidental durante varias operaciones que exigían la laparotomía, estudios roentgenológicos de la circulación porta intrahepática—la llamada venografía porta. El procedimiento consiste en la introducción de un catéter de politeno en la vena porta, por una de las afluentes de la misma, y la rápida inyección por dicho catéter de 20 c.c. de diodrasto de 35 por ciento, después de lo cual se toma una radiografía.

Ese procedimiento ha resultado ser técnicamente factible y relativamente inocuo. Ha facilitado con bastante constancia venogramas satisfactorios de la porta, que parecen apoyar el concepto de un flujo corriente en dicha vena.

La aplicación práctica de la venografía porta al diagnóstico aguarda la determinación de las desviaciones de lo normal que puede reconocer el procedimiento en presencia de alteraciones patológicas en el hígado.

DISCUSSION

J. Edward Kearns, M.D. (Evanston, Ill.): I would like to ask Dr. Bridenbaugh if they have been able to demonstrate any tumors of the liver at the operating table. This would be of tremendous assistance to the surgeon.

It is of interest to hear about thorium again. My first introduction to thorium (1938) was as a diagnostic agent to demonstrate breast lesions. Since as surgeons we always amputated the breast after study, there was no question of tissue retention.

Leo G. Rigler, M.D. (Minneapolis, Minn.): Dr. Thomas' paper and Dr. Bridenbaugh's paper brought to my mind the influence of the surgeons upon our efforts. We started doing hepatosplenography in 1931. I think we were among the first in the United States to use thorotrast for this purpose, largely because our surgeons were confronted with a great many patients with carcinoma of the stomach or rectum. Many had metastases to the liver, not diagnosed currently; the surgeons were invading the abdomen and backing out rapidly at that time, and they wanted to know ahead of time whether they should explore some of these cases. We felt under the circumstances that use of this material was justified even though there was a question raised as to its safety. I think we did 400 cases or more and I must say that, while we abandoned using it, we found very little clinical difficulty on which we could put our finger.

The type of case cited by Dr. Thomas, in which there are petechiae can, of course, occur from any colloidal emulsion; it has nothing to do with thorotrast *per se*.

We reported a large series in which we studied the liver of patients who came to autopsy. I think it should be borne in mind that people who die of debilitating diseases, as many of these do, because the material is given particularly in patients with carcinoma, are likely to have necrosis of the liver; such phenomena are assigned to the thorotrast but are not necessarily due to it.

We studied a series of cases most intensively with regard to liver function and in none of those that we saw five years after the injection of the material—not as long an interval as in some of Dr. Thomas' cases—were we able to find any disturbance of liver function whatever, by the most exhaustive liver tests. We did, however, find elevated radioactivity by means of a counter on the abdomen, but at a very low level, probably of no great significance.

During the course of time our surgeons came to the idea that palliative removal of carcinomas of the stomach or rectum should be done even though metastases were present, so that the prime necessity for determining the presence of metastases preoperatively was lost to some degree and the procedure was discontinued.

In more recent years the surgeons are removing portions of the liver in which metastasis is present, and again it has become necessary to find out whether there are deep-seated metastases in the liver that cannot be observed even in the operating room. To some degree this was the stimulus for Dr. Moore's and Dr. Bridenbaugh's efforts, since the patients were going to be available for surgery in any case and, by this means, metastases might be found which were not visible on the surface of the liver and thereby give the surgeon an indication as to whether he had any opportunity at all to remove metastatic tissue present in the liver.

There are, of course, many other indications for the procedure that Dr. Bridenbaugh has outlined. I think perhaps it will be an excellent method in many cases for studying thrombosis of the splenic vein and other types of obstruction of the portal vein circulation.

We have had a good deal of experience with oil compounds for visualization of the liver. After hearing of Degkwitz's original production of an emulsified iodized oil which he felt would produce adequate visualization of the liver and spleen, we undertook some experiments of the same kind but we could not get enough of the compound into an animal to obtain satisfactory visualization without killing it.

As I think Dr. Thomas implied, in Sweden there have been about nine deaths from the use of the material that Degkwitz produced, and it has been abandoned. Since then, Olsson, in Sweden, has produced another compound having an affinity for fat, which is excreted by the liver and for which they have very great hopes.

Dr. Thomas (*closing*): There is one thing I should like to make clear. The untoward changes which we demonstrated were due to alpha rays. These alpha rays I mentioned as being demonstrated on the slide of the gallbladder submitted by Dr. Kerman of Oak Ridge to Dr. Pirkey. This shows definitely and in a most striking manner the ionizing tracks that are present in sufficient number to produce a very unhappy effect.

The contrast medium introduced by Olsson is brominated sesame seed oil, which was given orally.

Dr. Bridenbaugh (*closing*): In answer to Dr. Kearns' question, we have not as yet been able to demonstrate tumors of the liver at the operating table. We have, however, attempted portal venography in several cases in which known liver metastases were present. For what we believe were technical reasons only, these attempts were not successful.

Portal Venography

Preliminary Report[1]

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New York, N. Y.

EARLY IN 1948, a series of experiments was initiated in the Department of Surgical Research of the New York Hospital-Cornell Medical Center, with the ultimate purpose of determining whether the portal vein in man could be resected were it found to be invaded by a malignant tumor. Because, in contradistinction to the common laboratory animals, the anatomical relationships of this vessel in the *Macaca mulatta* monkey are almost identical with those of man, this animal was chosen for these studies. Within a few months, it was demonstrated that in the majority of instances sudden and complete occlusion of the portal vein of this monkey could be successfully accomplished. Emboldened by these animal experiments, the authors deliberately ligated the portal vein in two human beings suffering from inoperable gastric cancer. These patients ultimately died of their malignant neoplasms, but no untoward effects were noted which could be ascribed to the sudden and complete occlusion of their portal veins. The details of these experiments have been reported elsewhere (1–3).

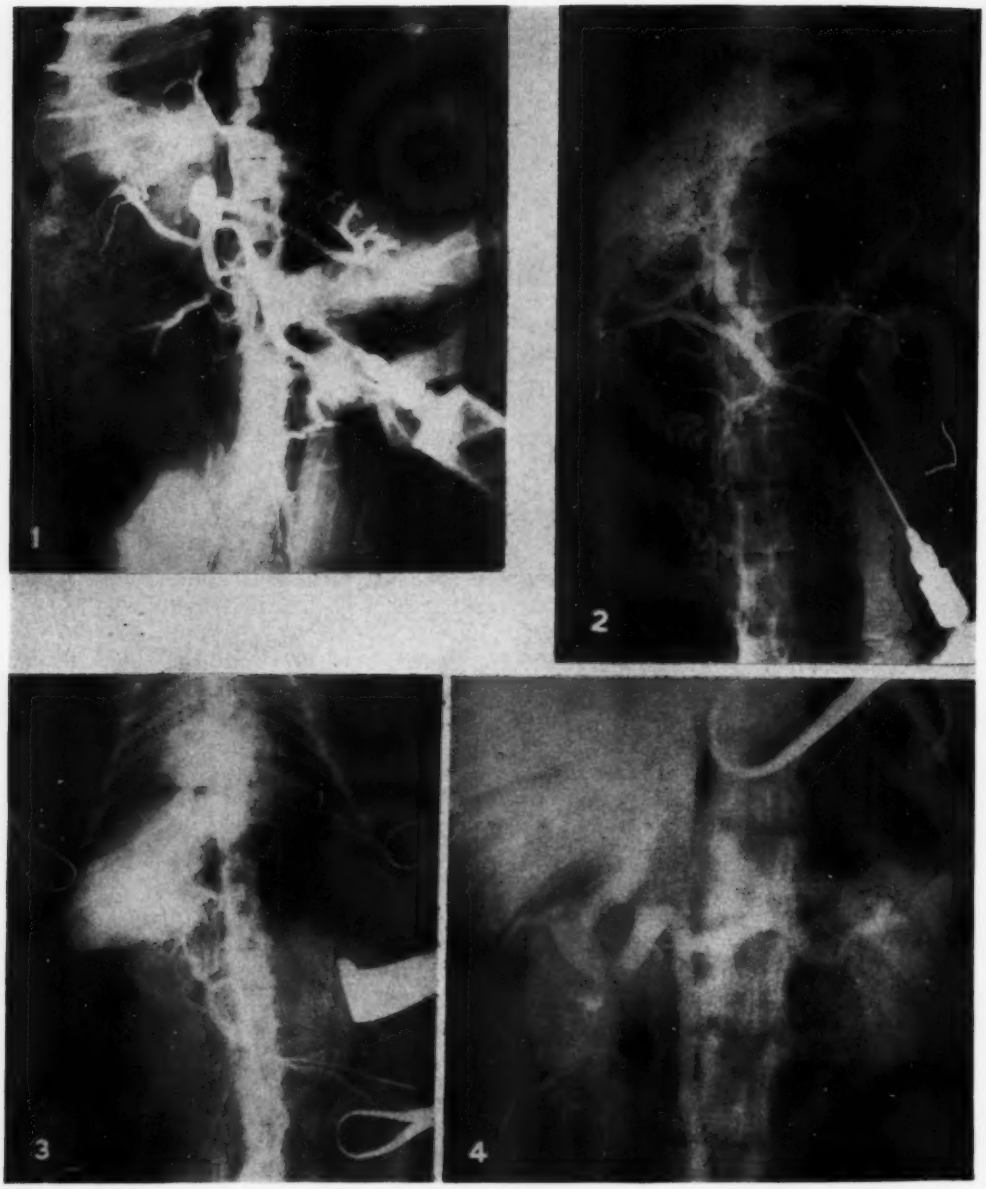
Relatively soon after these studies were begun, it became apparent that evaluation of the circulatory changes produced was unsatisfactory if the conventional methods of investigation were employed. Exploratory celiotomy, autopsy, and latex or metallic mass injections proved equally inadequate. The more dynamic technic of roentgen angiography after the injection of diodrast was, therefore, applied to this circulatory system and designated portal venography (1–3). This method of studying circulatory changes in the portal venous system has proved pre-eminently satisfactory both in the experimental animal and in man. It is the purpose of the present report to describe our experiences with this form of venous angiography and to comment upon its possible usefulness as a diagnostic procedure.

Only three other articles dealing with portal venography have been found. Fariñas (4), in 1947, published a venogram obtained after injecting diodrast into the saphenous vein of a patient who had apparently had a portacaval shunt performed for portal hypertension. Fariñas believed he demonstrated the portal vein and the liver. Blakemore (5) injected the same contrast medium into the coronary vein. He commented as follows: "Venography following the injection of. . . Diodrast in a branch of the coronary vein is useful in confirming the site of origin of the coronary vein." In 1950, Moore and Bridenbaugh (6) described their technic for visualizing the intrahepatic portal system and indicated that the practical applications of portal venography remained to be determined.

PRELIMINARY ANIMAL EXPERIMENTS

Portal venography has been performed in over 30 *Macaca mulatta* monkeys weighing from 10 to 20 pounds. In those animals in which the portal system has been injected rapidly with from 15 to 25 milliliters of 35 per cent diodrast, there have been no fatalities. Nor, as judged from serial liver biopsies and repeated liver function tests, has any hepatic damage been produced by the procedure. Two animals, in which 50 ml. of 70 per cent

[1] From the Department of Surgical Research, the Department of Surgery, and the Department of Medicine of the New York Hospital-Cornell Medical Center. This study was supported by a grant-in-aid from U. S. Public Health Service. Accepted for publication in April 1951.



Figs. 1–4. Portal Venograms in *Macaca mulatta* Monkey.

Fig. 1. Portal venogram obtained immediately after sudden and complete occlusion of the portal vein by ligature. The coronary, splenic, inferior and superior mesenteric veins, and portal stump are clearly demonstrated.

Fig. 2. Portal venogram obtained twenty-two days after ligature of the portal vein. The development of collaterals which even at this early date produce direct filling of the liver is readily apparent.

Fig. 3. Portal venogram sixty days after ligature of the portal vein. Rapid filling of the liver directly is obvious.

Fig. 4. Portal venogram obtained many months after occlusion of the portal vein, showing a large channel, presumably the pancreaticoduodenal vein, which has neatly by-passed the site of occlusion. The liver is well filled, as is the spleen.

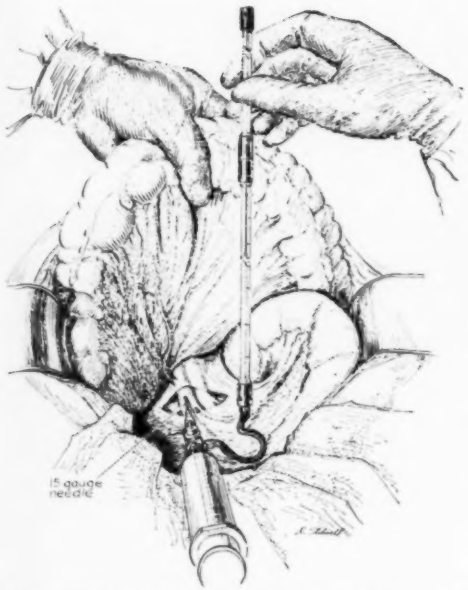


Fig. 5. Technic of portal venography. The superior mesenteric vein is exposed at the base of the mesentery of the transverse colon. The portal pressure is measured in centimeters of saline. Thirty-five per cent diodrast is injected directly through a No. 15 gauge needle.

diodrast was employed, died. One never recovered from the anesthesia. The other succumbed two days postoperatively in anuria. Such a dose as this is, of course, enormous as compared upon a basis of body weight with that which might be required in man. Figures 1, 2, and 3 are representative roentgenograms obtained in this monkey with the smaller doses. Figure 4 is a roentgenogram obtained with 50 milliliters of 70 per cent diodrast.

METHOD EMPLOYED IN MAN

In all of the human cases recorded below, the superior mesenteric vein has been isolated at the base of the mesocolon and injection has been performed through a No. 15 gauge needle. Forty milliliters of 35 per cent diodrast has been employed in all instances save one (Case 13), in which 50 ml. of 70 per cent diodrast was used. The contrast medium has been delivered manually from a 50 ml. Luer-Lok syringe and at as rapid a rate as possible. Neither have there been any fatalities, nor has any morbidity been detected which might be ascribed to the procedure.

Figure 5 illustrates the technic and site of injection. The spinal manometer shown has been an integral part of the equipment, for in all instances in which portal venography was considered of interest, measurements of portal pressure were routinely made. All roentgenograms have been obtained with a 15-ma. portable machine and a grid cassette. The exposure has always been made during the delivery of the last few milliliters of contrast substance. On numerous occasions in man, it was readily apparent that a more powerful x-ray machine was urgently needed if the full diagnostic potentialities of portal venography were to be realized.

CASE REPORTS

Portal venograms have been obtained in 21 patients during the course of an exploratory celiotomy or a definitive operation directed toward the cure of one or another intra-abdominal disease entity. Fourteen of the films obtained have proved of sufficient interest and definition to warrant their reproduction in this report. For convenience in presentation, these will be considered under the heading of the disease for which the patients were subjected to operation.

Acute Relapsing Pancreatitis

CASE 1 (Fig. 6): E. C., a 35-year-old, white, married female was admitted with a five-year history of recurrent attacks of acute pancreatitis. During the course of several of these bouts of anguishing pain, the serum amylase was found to reach levels as high as 1,100 units. At operation, the pancreas was found to be all but completely replaced by fibrous tissue. After cholangiographic demonstration of a fistulous tract between the common and pancreatic ducts, the pancreatic duct was divided and implanted into the adjacent duodenum. Shortly after cholangiography, the portal venogram reproduced in Figure 6 was obtained. The pressure within the superior mesenteric vein was 11 cm. of saline. The liver appeared quite normal.

Radiographic Interpretation: About the only conclusion that seems warranted from examination of this film is that it appears

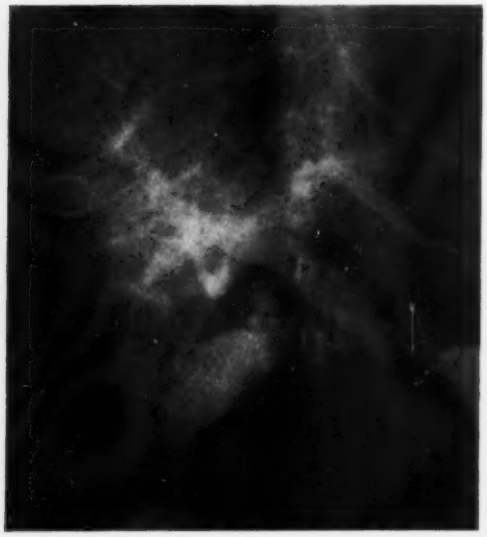


Fig. 6. Case 1: Acute relapsing pancreatitis; normal liver. The hepatic pattern obtained in this patient is believed to be normal. Visualization of the gallbladder and cystic duct is quite incidental, due to cholangiography performed a few moments prior to injection of dye into the portal vein.

to outline faithfully the normal portal vein (P.V.) and the intrahepatic portal venous system. At point SV the entrance of the splenic vein can be detected. At point X there appears to be a semicircular defect within the superior mesenteric vein. Since careful examination of this vessel at the time of operation failed to reveal any corresponding abnormality, the apparent failure of the vessel to fill is attributed to the abnormal currents set up within it by the forceful injection of the contrast medium. We interpret this as a normal portal venogram.

Portal Hypertension Due to Cirrhosis of the Liver

CASE 2 (Fig. 7): D. K., a 38-year-old, single, white female, was admitted to the hospital complaining of weakness, loss of weight, and a probable hematemesis. Esophageal varices were demonstrated during the course of a gastro-intestinal series, and the stools were positive for blood. At operation, the portal pressure was found to be 37 cm. of saline, and the portal venogram reproduced in Figure 7 was obtained. Following an end-to-side anastomosis between the portal vein and vena cava, the portal pressure fell to 22 cm. of saline. A biopsy revealed extensive cirrhosis of the Laennec variety.

CASE 3 (Fig. 8): S. L., a 47-year-old housewife, was admitted with a long history of excessive alcoholic intake and two known bouts of severe esophageal hemorrhage. Varices were demonstrated upon the esophagram. The portal venogram shown in Figure 8 was obtained and an end-to-side portacaval shunt was performed, reducing the portal pressure from 47 to 26 cm. of saline.

Fig. 7. Case 2: Cirrhosis of the liver. The most striking feature in this film is the marked enlargement of the right lobe of the liver as indicated by the length of the right hepatic vein. Whether the apparent failure of the small venous radicles to fill is diagnostically significant cannot be determined at this time.

Radiographic Interpretation (Cases 2 and 3): In both of these cases there was definite roentgenologic evidence of enlargement of the liver as judged by the extent of the venous pattern. In Case 2 (Fig. 7), there is a remarkably long vein extending down into a greatly enlarged right lobe, while in Case 3 (Fig. 8), the hepatic enlargement appears more diffuse. There is a temptation to call attention to the fact that the smaller intrahepatic veins seem less well filled in these two cases than in Case 1. Furthermore, it would appear that the main intrahepatic trunks are of a smaller caliber than those seen in Case 1. To draw any diagnostic conclusions from these observations would, of course, be quite unjustified at the present time. In

these two cases, no satisfactory explanation can be advanced for the difference in filling of the splenic and inferior mesenteric vessels unless this be upon the basis of unappreciated variations in injection rates and pressures.

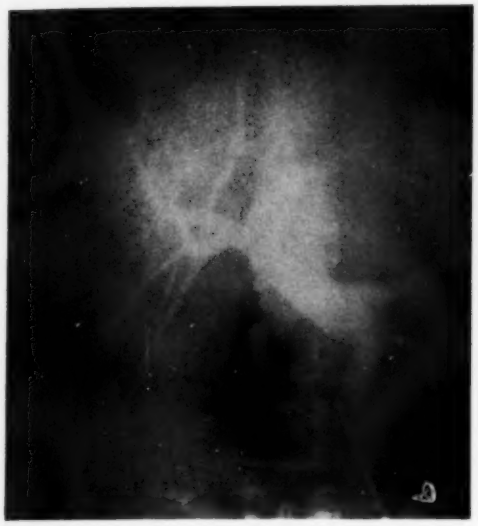


Fig. 8. Case 3: Cirrhosis of the liver. As in Fig. 7, the significant feature here is the increase in size of the liver. In this case, it appears more diffuse rather than being confined to the right lobe as in Fig. 7. When this venogram is compared with one presumed to be normal (Fig. 6), a decrease in caliber of the intrahepatic veins is evident, and the terminal capillary bed is not filled. Judgment as to the significance of these findings must be reserved.

CASE 4 (Fig. 9): E. D., a 40-year-old, white, married female with a six-year history of biliary cirrhosis, was admitted during a severe episode of esophageal hemorrhage. The bleeding was controlled by esophageal tamponade with a Sengstaken-Blakemore balloon (7) and the patient was subjected to operation. The portal venogram reproduced in Figure 9 was obtained and an end-to-side portacaval shunt performed. After the shunt had been opened, the portal pressure fell from 46 to 20 cm. of saline. The long preoperative course in this case and innumerable detailed studies have been reported elsewhere (8—case identified as Patient 11).

Radiographic Interpretation: For this venogram, a different technic was employed. This consisted in temporarily occluding the portal vein at the portal fissure (4) and then injecting the diodrast. The purpose of this variation was to demonstrate, if possible, the course of the esophageal varices. Although this unfortunately failed in this patient, the film is exhibited in Figure 9 for what interest it may have. The portal vein is nicely filled (P.V.), and the inferior mesenteric (I.M.), splenic (SP), and coronary (C) are outlined faintly.

Fig. 9. Case 4: Cirrhosis of the liver. Here the portal vein was temporarily occluded at point X prior to injection of diodrast. This variation in technic was directed toward the demonstration of the esophageal varices. Although a failure from this point of view, this film is reproduced here for what interest it may have.

Sudden and Complete Occlusion of the Portal Vein in Inoperable Gastric Cancer

CASE 5 and CASE 6 (Figs. 10 and 11): Upon exploratory celiotomy, both of these patients, F. W. and A. L., were found to have inoperable gastric cancers. After sudden and complete occlusion of the portal vein with a heavy silk ligature, the venograms reproduced in Figs. 10 and 11 were obtained.

Radiographic Interpretation: Little by way of comment is required here other than to point out how faithfully the major portal tributaries are outlined. Incidentally, it is interesting to compare these films, obtained following sudden portal occlusion, with those of patients with pancreatic cancer, in whom the obstruction can be presumed to have been gradual. Cf. Figures 12–15.

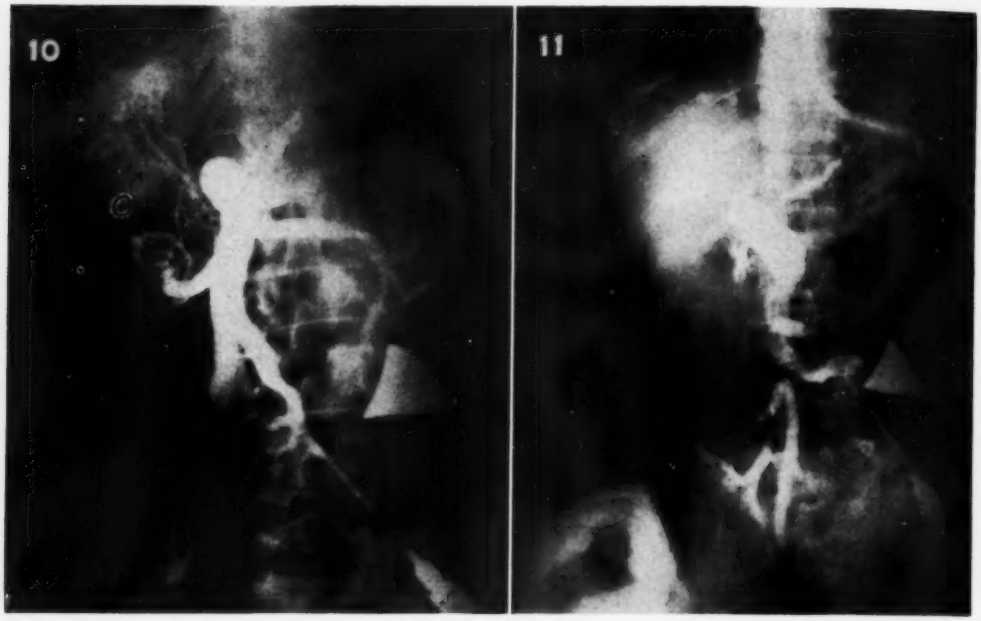


Fig. 10. Case 5: Inoperable gastric cancer. In this case and Case 6 (Fig. 11), the portal vein was occluded by a silk ligature at the portal fissure. This film is of particular interest for, in addition to outlining the portal system, it demonstrates collaterals (C) which succeed in immediately returning blood to the liver.

Fig. 11. Case 6: Inoperable gastric cancer. In this film again the portal venous system is outlined after complete occlusion at the portal fissure. The diffuse increased density in the area occupied by the right lobe of the liver is interpreted as due to diodrast in the terminal hepatic capillaries. Presumably the dye has reached the liver through collaterals too small to visualize. Comparison of these two films with Fig. 2 indicates how similar is the portal circulation in man and the *Macaca mulatta* monkey.

Cancer of the Head of the Pancreas

The next four portal venograms (Figs. 12–16) were all obtained in patients with adenocarcinoma of the head of the pancreas. In 2 (Cases 7 and 10) radical pancreaticoduodenectomy was performed; in 2, the tumors were inoperable.

Radiographic Interpretation: In *Case 7* (Fig. 12) a large, bulky tumor without evident metastases was disclosed as soon as the abdomen was opened. The portal venogram was interpreted as revealing displacement of the portal vein to the left without evidence of direct invasion by the neoplasm. This was confirmed during the course of dissection. The tumor was easily removed from the portal and superior mesenteric veins, and no evidence of infiltration could be detected.

In *Case 8* (Fig. 13) a large tumor of the head of the pancreas was readily identified at operation. There were numerous small hepatic metastases. Here, in an effort to secure better filling of the junction of the portal and superior mesenteric veins, the portal vein was partially occluded (X). The venogram in this case is interesting for several features: first, there is no evidence of a portal vein which can be identified as such; second, the circular area (T) outlined by the pancreaticoduodenal vein corresponds exactly with the position of the tumor; third, extensive collaterals in and about the head of the pancreas have apparently developed secondary to the portal block. Consistent with this demonstration of a portal block is the fact that the portal pressure was 34 cm. of saline. This film is interpreted as offering conclusive evidence of invasion of the portal vein by malignant neoplasm.

At operation in *Case 9* (Fig. 14) a large mass was discovered in the head of the

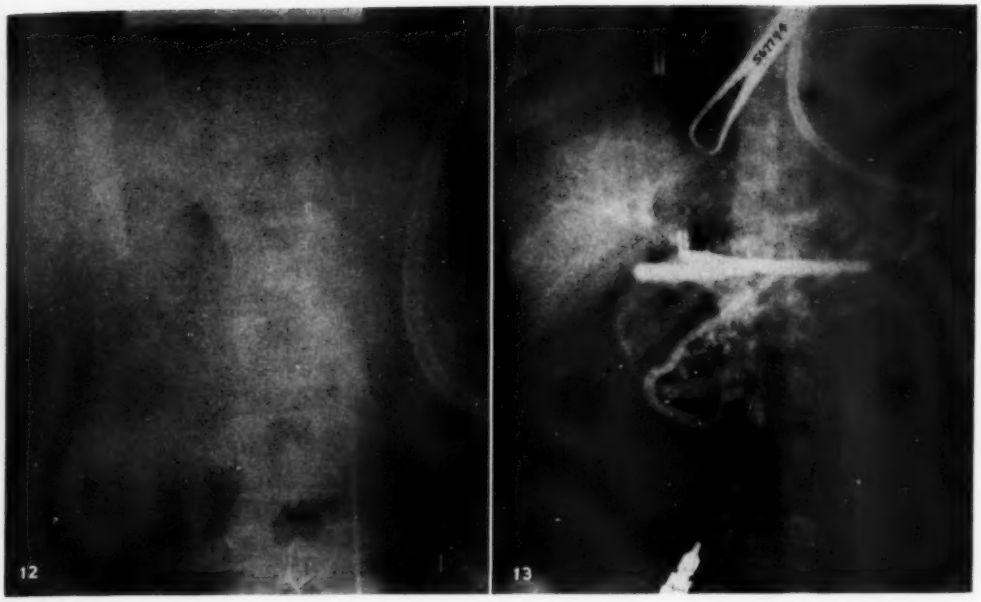


Fig. 12. Case 7: Carcinoma of the pancreas. This film reveals a smooth, crescentic defect due to extrinsic pressure. The portal and superior mesenteric veins are displaced a centimeter or two toward the patient's left. There is no evidence of invasion of these vessels by tumor.

Fig. 13. Case 8: Carcinoma of the pancreas. In this film, the tumor is outlined (T) and the extensive collaterals are well demonstrated. This is considered an example of extensive invasion of the portal vein by cancer.

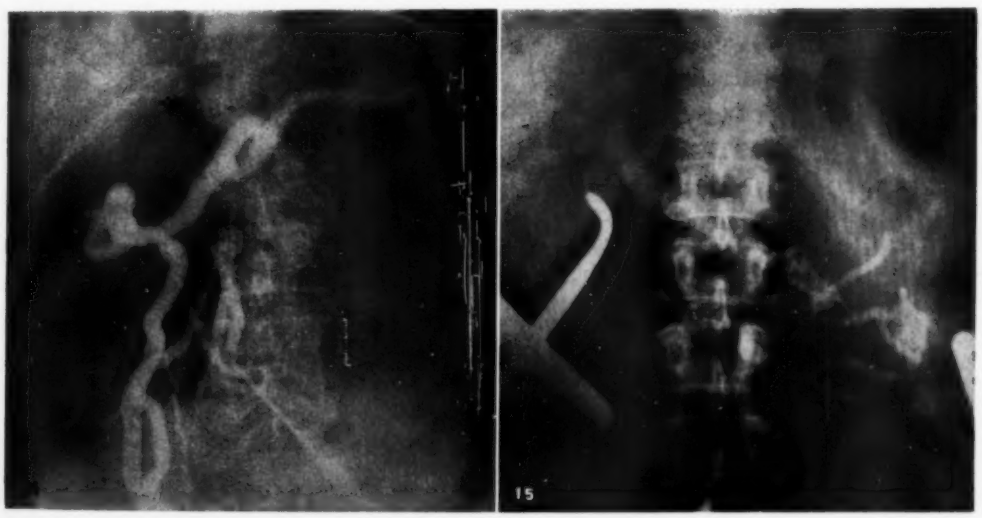


Fig. 14. Case 9: Carcinoma of the pancreas. This venogram reveals complete obstruction due to cancer invading the superior mesenteric vein.

Fig. 15. Case 10: Carcinoma of the pancreas. Invasion of the portal vein by tumor, confirmed both at operation and autopsy.

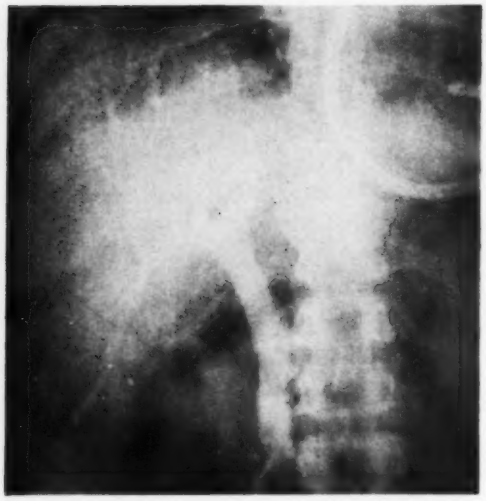


Fig. 16. Case 11: Chronic cholecystitis and cholelithiasis; jaundice. This, in light of present knowledge, is considered to be a normal portal venogram. Cf. Fig. 6.

pancreas. The regional lymph nodes were filled with tumor, and there were numerous metastatic deposits in the liver. The portal venogram is interpreted as revealing complete obstruction of the portal vein. The large, tortuous collaterals, though not positively identified, are thought to be the right and left colic veins. The catheter in the left upper field of the plate was loosely looped about the portal vein for identification purposes. Of some interest here is the fact that the portal vein obviously contains a small amount of the contrast medium. We can only postulate that this gained access to the vessel through collaterals too small to visualize. In this patient, the portal pressure was 24 cm. of saline, a figure lower than would be expected in the face of total portal obstruction. Another important observation is that there is no filling of the splenic or inferior mesenteric veins. The major point of obstruction then, in this patient, can be placed at the junction of these vessels as they fuse to form the portal.

In *Case 10* (Fig. 15), shortly after the peritoneal cavity was entered, a moderate sized carcinoma of the head of the pancreas was demonstrated. There were no demonstrable regional or distant metastases, and on palpation the portal and superior mesenteric veins were thought to be free of tumor. When, however, in the course of radical pancreaticoduodenectomy, an effort was made to dissect the mass from these vessels, it became obvious that they were directly invaded by cancer. Although the operation was completed successfully, it was the surgeon's opinion that tumor had been left behind in the walls of the superior mesenteric and portal veins. In view of the operative findings, Figure 15 is of particular interest. It obviously reveals a marked disturbance in the normal portal pattern which can, in our opinion, only be interpreted as due to invasion by tumor. This patient died on the sixty-seventh postoperative day, and at autopsy the entire portal vein was found to be invaded and compressed by tumor. There was no evidence of neoplasm growing free within the lumen of the vein.

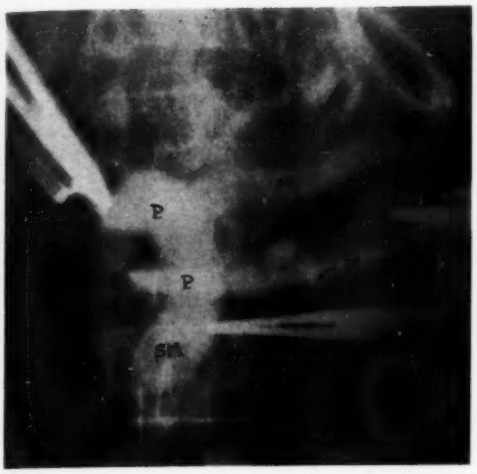
Chronic Cholecystitis and Cholelithiasis: Jaundice

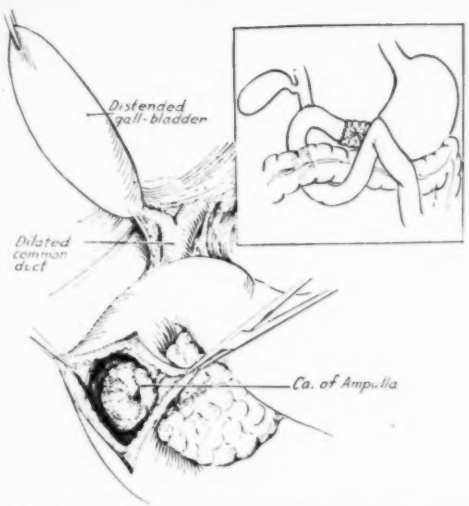
CASE 11 (Fig. 16): E. W., a 47-year-old, married, white female, was admitted with a typical history of chronic gallbladder disease of many years duration and of jaundice for three weeks. At operation, a large, chronically diseased gallbladder was identified. In spite of the jaundice, common duct exploration was negative.

Radiographic Interpretation: The portal venogram, like that in Figure 6, presents what is believed to be a faithful outline of a normal portal vein and intrahepatic venous system. The portal pressure was 13 cm. of saline.

Carcinoma of the Ampulla of Vater

CASE 12 (Fig. 17): F. P., a 66-year-old, white male, was admitted to the hospital because of jaundice of two months duration. Physical examination was negative save for moderate enlargement of the liver and jaundice. Several stool examinations were strongly positive for occult blood. At operation, a sharply circumscribed, non-infiltrating papillary carcinoma of the ampulla was readily identified, and a radical pancreaticoduodenectomy was performed. Just prior to embarking on this radical procedure, the portal venogram reproduced in Figure 17 was obtained. Figure 18 is an artist's conception of the tumor in this case. The patient died upon the fourteenth postoperative day. The postoperative





Figs. 17 and 18. Case 12: Carcinoma of the ampulla of Vater. The venogram, obtained with the portal vein occluded, fails to reveal any intrinsic or extrinsic defect in the superior mesenteric or portal vein.

The drawing is the artist's concept of the tumor. The insert depicts the manner in which the gastro-intestinal tract was reconstructed following radical pancreaticoduodenectomy.

survival period was characterized first by oliguria and then by profuse gastro-intestinal hemorrhage. At postmortem examination, the source of the repeated hemorrhages could not be found, and microscopic examination of the kidneys led the pathologist to make a diagnosis of so-called shock kidney (frequently referred to as lower nephron nephrosis). Although diodrast was thought of as a possible explanation of this untoward series of events, it hardly seems likely that this patient's death can be ascribed to its use.

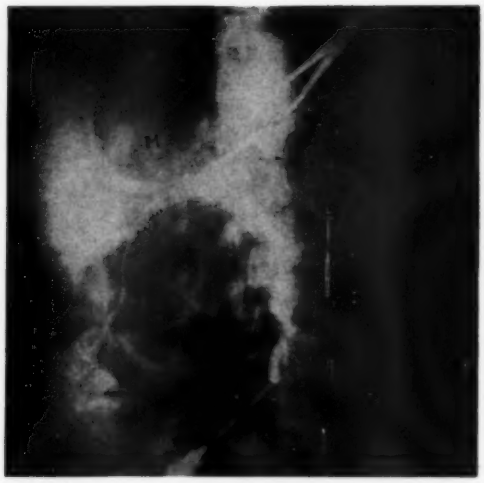


Fig. 19. Case 13: Carcinoma of the gallbladder with hepatic metastases. This film reveals a large tumor (T) in the right upper quadrant and an enormous hepatic metastasis (M).

Radiographic Interpretation: The portal venogram was obtained with the vessel occluded at the portal fissure. The purpose of this technic is, of course, to obtain better filling of that portion of the vein most likely to be the site of carcinomatous infiltration. The film clearly delineates the superior mesenteric, the portal, the coronary (C), the splenic (SP), and the inferior mesenteric (I.M.) veins. There is no evidence of an intrinsic defect nor of extrinsic pressure. The apparent crescentic course taken by the portal vein is not believed to be due to pressure exerted by the tumor, but rather to distortion occasioned by the temporary occlusion of the vein. On the basis of the information provided by this venogram, the radical operation was embarked upon without hesitation. The portal vein was found free of tumor at the time of operation, as well as at autopsy performed two weeks later.

Primary Cancer of the Gallbladder, with Large Hepatic Metastasis

CASE 13 (Fig. 19): S. S., a 42-year-old, married, white housewife, was admitted with a history of right upper quadrant pain of four weeks duration. Physical examination revealed a deeply jaundiced woman whose liver was palpable three finger breadths below the right costal margin. At explor-

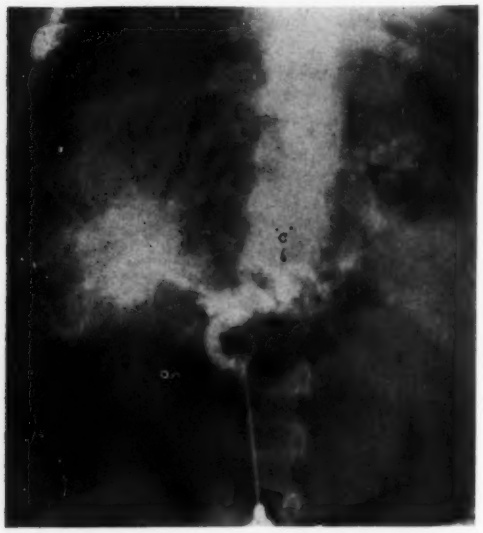


Fig. 20. .Case 14: Portal hypertension due to extrahepatic block. In this film is demonstrated an extrahepatic portal block. The portal vein proper has been replaced by multiple collaterals which presumably have developed in the region of the hepatoduodenal ligament. The origin of the splenic vein is visualized. The tortuous vessel marked C is probably the coronary vein.

atory celiotomy, the region of the gallbladder and common duct was found to be occupied by a large, irregularly lobulated tumor. The liver was the site of many large, metastatic deposits. The portal pressure was measured at 24.5 cm. of saline, and the portal venogram reproduced in Figure 19 was obtained with 50 milliliters of 70 per cent diodrast.

Radiographic Interpretation: This film reveals a distinctly abnormal swing in the portal vein as it skirts the large mass in the right upper quadrant (T). Of additional interest is the spherical intrahepatic defect corresponding exactly to the large metastasis which was identified at the operating table (M). Whether the apparent intrinsic defects along the inferior border of the portal vein are due to invasion by tumor or currents within the vessel cannot be determined.

Portal Hypertension due to Extrahepatic Block

CASE 14 (Fig. 20): W. D., a boy of five and a half years, was admitted to the hospital because of repeated esophageal hemorrhages over a period of one year. His past history was of interest in that at the age of six weeks he suffered from a severe purulent omphalitis which, however, subsided within a week upon appropriate antimicrobial therapy. On admission, the child was pale, and his spleen was palpable at the level of the umbilicus. An esophagram revealed many varices. Liver function tests were normal.

At operation, innumerable vascular adhesions were encountered in the entire right upper quadrant. These obscured the gallbladder and common duct. The omentum was densely adherent to the inner aspect of the anterior abdominal wall, particularly in the region of the umbilicus. The pressure in the superior mesenteric vein was 47 cm. of saline. The portal venogram is reproduced in Figure 20. Following removal of the spleen, the pressure in the portal system, measured in the splenic vein, had fallen to 42 cm. of saline. After establishment of an end-to-side splenorenal shunt, the pressure in the splenic vein was 36 cm. of saline.

Radiographic Interpretation: The venogram in this case is interpreted as revealing replacement of the portal vein proper by innumerable small collaterals in and about the head of the pancreas and hepatoduodenal ligament. It proved of great value during operation by clearly indicating that any anastomosis employing the portal vein would be impossible. Any effort, therefore, directed toward lowering the pressure in the portal system would of necessity have to involve removal of the spleen and a splenorenal shunt. In the film, the liver is seen to be lightly filled and appears normal in size. The junction of the splenic and superior mesenteric veins is clearly delineated. The small puddles of contrast substance lying just below the left diaphragm are believed to represent dilated veins at the gastric cardia. Whether these have filled through the coronary or through the splenic vein cannot be determined. It is believed that the relatively large vein which presents as an inverted "U" is the coronary, for faintly outlined just below is a shadow which may well be the splenic.

SUMMARY AND CONCLUSION

A detailed review of eighteen portal venograms, 14 in man and 4 in the *Macaca mulatta* monkey, has been presented. Those in man have been performed in the course of either an exploratory celiotomy or a definitive surgical procedure. The technic employed is described.

Any final evaluation of the diagnostic worth of portal venography as performed in this clinic must await the accumulation of additional experience. At the present time, however, it is believed that the procedure is a simple one which does not add significantly to the over-all surgical risk. In several instances, particularly in those patients with pancreatic cancer, this form of angiography has already demonstrated its value. In our research laboratory, portal venography has proved valuable in studying the dynamics of this circulatory system. Actually, it proved the only practical method for demonstrating changes produced by various surgical maneuvers.

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SUMARIO

Venografía Porta. Comunicación Preliminar

La venografía porta, como método para estudiar las alteraciones circulatorias en el sistema venoso de la porta, ha resultado satisfactoria, tanto en los animales de experimentación (monos *Macaca mulatta*) cuanto en el hombre. La técnica empleada comprende aislamiento de la vena mesentérica superior en la base del mesocolon e inyección con la mayor rapidez posible de 40 mililitros de diodrasto al 35 por ciento con una aguja de calibre 15. Las exposiciones a los rayos X tienen lugar durante la introducción de los últimos mililitros del medio de contraste. En algunos casos, se modifica la técnica, ocluyendo la vena porta antes de inyectar el diodrasto.

Obtuviéronse venogramas portales en 21 casos durante el transcurso de una celiotomía exploradora o de algún procedimiento quirúrgico bien definido, reproduciéndose aquí 14 de los mismos. Sirven éstos para ilustrar casos de pancreatitis recidivante aguda (venograma normal); hipertensión porta debida a cirrosis del hígado; cáncer gástrico inoperable; cáncer de la cabeza del páncreas; colecistitis y colelitiasis crónicas (venograma normal); carcinoma de la papila de Santorini; cáncer primario de la vesícula biliar con metástasis hepáticas; hipertensión porta debida a bloqueo extrahepático.

Toda valuación definitiva de la venografía porta, tal como se describe aquí, tiene que aguardar el acopio de más datos. No obstante, en la actualidad parece que el procedimiento es sencillo y no acrecienta mayor cosa el riesgo quirúrgico general. En varios casos, y en particular en los enfermos con cáncer pancreático, esta forma de angiografía ya ha demostrado su valor.

Treatment of Radiation Sickness with ACTH

A Preliminary Report of Fourteen Cases[1]

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THE ANTERIOR pituitary adrenocorticotropic hormone (ACTH) is being used effectively for the relief of radiation sickness in those patients who are refractory to the usual methods of its treatment. These are discontinued before starting the intramuscular injections of the hormone. The results in the first 14 patients exclusively treated by ACTH are given in the hope of stimulating further investigation along this line.

In order to show that the relatively small amounts of ACTH being administered to these patients are sufficient to have a real effect, white mice were exposed to lethal amounts of total body roentgen radiation and subsequently treated with ACTH in doses comparable in milligrams per gram of body weight to those used in man.

THE PREMISE AND THEORY

The hypothesis that ACTH would alleviate radiation sickness was originally conceived on the premise that the symptoms of this condition may be caused by intoxication from tissue decomposition products resembling histamine, as indicated by relief observed in the past following administration of such anti-histaminic drugs as benadryl in some patients and adrenocortical hormone in others. If the latter relieves the nausea and vomiting (1), it seems logical to stimulate the patient's own adrenal cortex to produce more of its hormone. If roentgen irradiation is another stress which produces the "alarm reaction" of Selye (2) in patients not already debilitated by their cancer, it would seem logical to bridge them over their "stage of exhaustion," which might be represented by radiation sickness.

ACTH stimulates the normal adrenal cortex to produce glucocorticoids, including cortisone, which appear to support the replenishment of energy stores, electrolytes and water, to render the body capable of reacting adequately, physiologically, to continued stress situations such as burns, anoxia, fractures, extreme environmental temperatures or pressures, and shock (3). To these situations, I wish to add radiation sickness.

ACTH should, as a rule, be preferable to cortisone for two reasons. First, ACTH would stimulate a more constant production of cortisone as compared to the peaks of concentration in the tissues which result from intermittent injections. Secondly, ACTH usually causes hypertrophy and hyperplasia of the adrenal cortex (4), with continuance of increased function for a short time after administration has been discontinued, whereas the effect of cortisone on adrenal cortical structure is just the opposite (4). The effects of ACTH depend, however, upon the sensitivity of the adrenal cortex to its stimulation (3). If the cortex is insensitive, as in Addison's disease, little benefit is gained from trying to bring it back (5). In this case, of course, cortisone is preferable to ACTH.

Twenty-five years ago, while I was studying with Evans, he showed that injections of pituitary extract were followed by hypertrophy of the adrenal gland in laboratory animals (6). Sprague *et al.* (4) have recently reported hypertrophy and hyperplasia of the cortical tissue in man following administration of ACTH. Mason *et al.*, (7), Forsham, *et al.* (8), and others (9) have shown that crystalline ACTH stimulates the adrenal cortex to greater function in normal human subjects. Ellis (10) advanced the theory of histamine intoxication as a cause of radiation sickness, a theory which has been

[1] Accepted for publication in February 1951.

popularized by Ellinger (1), who stresses the anti-histaminic effect of the adrenocortical hormone. Ellinger states that desoxycorticosterone acetate relieves nausea and vomiting in most cases, and he believes that radiation sickness is due to adrenal insufficiency. Patt (11) disagrees, but reports that 45 per cent of 30 hypophysectomized white rats died three or four days after receiving 750 r of roentgen radiation, while unoperated controls lived six days or more. Lofstrom and Nurnberger (12) subscribe to Ellis' theory and have also found benadryl efficacious in treating radiation sickness.

In addition to these concepts as a basis for this study, there are several effects of ACTH (8, 9, 13), each of which has been shown in the past to help alleviate or prevent certain conditions which also constitute some of the untoward effects of ionizing radiations. ACTH usually causes retention of sodium chloride (8). Markovits (14) and Steinberg (15) reported increased susceptibility to x-ray sickness in patients with sodium chloride starvation and obtained a favorable response following administration of NaCl. Steinberg focused attention on the fact that radiation sickness is more pronounced if marked secondary anemia is present. White and Dougherty (16), on the other hand, found that ACTH produced a return of the red cells to normal. Shock has been compared with radiation sickness by Jenkinson and Brown (17), who suggested treating it with drugs which maintain the peripheral circulation and prevent viscerostasis and splanchnic dilatation. Painter *et al.* (18) stated that adrenalin protects against the lowering of blood pressure in irradiated rabbits and suggested that it should be useful in therapy. Abelson and Moyes (19) showed that epinephrine stimulates the pituitary-adrenal cortex system.

The possibility that there may be contraindications to the use of ACTH in patients receiving total body irradiation must be kept in mind. Cronkite (20) suggests, for example, that the sodium chloride and water retention might do harm in these cases. Ragan (9) reported absence of granulation tissue and failure of wounds to heal in patients being treated with ACTH. I have noted that the recovery rate of the skin was decreased in the two patients (Cases 3 and 5) listed in Table I who received larger doses of ACTH than I usually administer. However, the smaller doses effective in treating radiation sickness in most instances do not appear to be sufficiently large to interfere with tissue recovery. Of course, ACTH in larger doses reduces the circulating lymphocytes (9), to add insult to radiation injury if injudiciously used.

CASES SELECTED AND FACTORS USED

Only those patients who were treated exclusively with ACTH after other methods of treatment had been discontinued and who have now completed their radiation therapy have been selected for this report. Most of them had received intensive x-ray therapy for several weeks before becoming sufficiently ill to warrant the ACTH treatment. All were treated over the torso. Most of them were given 200 r (in air) of hard x-rays (h.v.l. 4 mm. Cu) daily or thrice weekly through sizable ports (10 × 15 cm., more or less) totaling 2,000 r per port (in air). In Table I the amount is expressed also in volume dose or integral dose[2] for comparison; but this figure, of course, is affected by variations in tissue recovery with different time intervals, degree of protraction, etc., which probably contribute to the wide variation in the number of megagram-roentgens producing radiation sickness in different individuals. This is to say nothing of the differences in radiosensitivity of the various anthropologic types of patients (21) and a host of other biological factors which might influence the reaction of human subjects to radiation, all of which are far beyond the scope of this paper.

[2] Volume dose or integral dose is the total amount of energy absorbed by the patient as estimated from depth dose curves and the volume of tissue irradiated. One gram-roentgen is the amount of energy absorbed by one gram of tissue when traversed by one roentgen (Quimby).

TABLE I: DATA ON FOURTEEN PATIENTS TREATED WITH ACTH

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Sex and age	F, 49	F, 58	F, 71	M, 58	F, 59	M, 63
Diagnosis	Ca of cervix, Stage II	Postop. Ca of breast, Stage II	Lymphosarcoma of stomach	Postop. Ca of bladder	Ca of cervix, Stage III	Postop. Ca of prostate
Roentgen therapy						
Areas treated	Pelvic ports (6) "Sacrosciatic" (2) Transvaginal	Chest, A. & P. Axillae Supraclavicular	Chest, A. & P. Abdomen, A. & P.	Pelvic ports	Pelvic ports (6) "Sacrosciatic" (2) Transvaginal	Pelvis Perineum Thigh
Size of ports	10 × 15 cm. 6 × 8 cm. 3.5 cm. diam.	10 × 10 cm. 10 × 15 cm.	15 × 15 cm.	10 × 15 cm.	10 × 15 cm. 6 × 8 cm. 3.5 cm. diam.	10 × 15 cm. 6 × 8 cm. 10 × 20 cm.
Number of ports	9	4	6	4	9	3
Dose per port per treatment (in air)	200 r 400 r	200 r	150 r	200 r	150 to 400 r	50 to 100 r
Interval between treatments	1 day	1 day	2 days	1 day	2 days	3 days
Volume dose per treatment (gram roentgens)	49,000	7,000 to 28,000	10,000 to 63,000	36,000	75,000 to 100,000	7,000 to 26,000
Total dose per port (in air)	2,000 r 4,000 r (vag.)	1,800 r	1,200 r	1,800 r	2,000 r 4,000 r (vag.)	1,000 r
Total megagram roentgens (all ports)	2.3	2.09	1.39	1.27	3.65	0.26
Clinical data						
Manifestations of radiation sickness						
Anorexia	+	+	+	+	+	+
Headache	+	−	+	−	+	−
Lassitude	+	+	+	−	+	+
Nausea	+	+	+	+	+	+
Vomiting	+	+	+	+	+	+
Diarrhea	+	−	+	+	+	−
Dizziness	−	+	−	−	+	−
Body weight						
Before irradiation	151 lb.	131 lb.	100 lb.	175 lb.	124 lb.	154 lb.
After irradiation and ACTH	151 lb.	130 lb.	98 lb.	170 lb.	114 lb.	150 lb.
Blood pressure (mg. Hg)						
Before ACTH	120/75	110/65	136/80	145/85	120/60	118/76
After ACTH and completion of irradiation	125/75	130/70	130/72	152/88	150/70	130/70
ACTH therapy data						
Duration of irradiation when radiation sickness started	21 days	8 days	12 days	18 days	8 days	19 days
Dose per port when sickness started	1,600 r	400 r	900 r	1,400 r	600 r	600 r
Megagram roentgens when sickness started	1.5	0.19	0.23	0.94	0.3	0.22
Interval between injections (10 mg. per injection)	1 day	2 days	2 to 15 days	2 days	2 days	3 days
Total dose of ACTH	30 mg.	30 mg.	145 mg.	60 mg.	85 mg.	25 mg.
Total time of ACTH therapy	3 days	7 days	49 days	21 days	21 days	21 days
Time required for subsidence of radiation sickness	4 days	8 days	4 days	23 days	37 days	22 days

METHOD OF TREATMENT WITH ACTH

The oral administration of Kapseals of ABDEC and of Combex with C, which we routinely supplement with pyridoxine hydrochloride and vitamin B-12 in some form, is usually discontinued due to inability of the patient to retain these when this "stage of exhaustion" from irradiation is reached, requiring parenteral administration. At this time, treatment with ACTH is begun.

The first patients to receive ACTH were given 5 mg. intramuscularly at each visit, either daily or on alternate days. These injections were found to be ineffective, an observation which is held to rule out the

TABLE I: DATA ON FOURTEEN PATIENTS TREATED WITH ACTH (*Cont.*)

Case 7	Case 8	Case 9	Case 10	Case 11	Case 12	Case 13	Case 14
F, 40	F, 61	F, 51	F, 62	F, 70	F, 49	M, 45	F, 30
Postop. Ca of breast, Stage II	Postop. epidermoid Ca of rt. inguinal node	Endometritis	Ca of cervix, Stage III	Postop. Ca of ovary	Ca of cervix, Stage II	Lymphosarcoma, generalized	Ca of cervix, Stage I
Chest, A. & P. Axillae Supraclavicular	Rt. inguinal Lower abdomen	Pelvic ports	Pelvic ports (6) "Sacrosciatic" (2) Transvaginal	Pelvic ports	Pelvic ports (6) "Sacrosciatic" (2) Transvaginal	All node-bearing areas	Pelvic ports (6) "Sacrosciatic" (2) Transvaginal
10 × 10 cm. 20 × 20 cm.	6 × 8 cm. 10 × 15 cm.	10 × 15 cm.	10 × 15 cm. 6 × 8 cm. 3.5 cm. diam.	10 × 15 cm.	10 × 15 cm. 6 × 8 cm. 3.5 cm. diam.	15 × 15 cm. 10 × 10 cm.	10 × 15 cm. 6 × 8 cm. 3.0 cm.
4	2	6	9	4	9	14	9
200 r	200 r	100 to 250 r	200 r	200 r	200 r	150 r	200 r
1 day	2 days	1 day	1 day	1 day	1 day	2 days	1 day
8,000 to 36,000	8,000 to 25,000	49,000	48,000	95,200	100,000	48,000 to 112,000	110,000
1,600 r	1,200 r	2,000 r	2,000 r 4,000 r (vag.)	1,600 r	2,000 r 4,000 r (vag.)	450 r	2,000 r 4,000 r (vag.)
1.29	1.35	2.3	2.81	1.5	2.72	2.28	2.82
+	+	+	+	+	+	+	+
−	−	−	+	−	−	−	−
−	+	+	+	−	−	+	−
+	+	+	+	+	+	+	+
+	+	+	+	+	+	+	+
−	−	−	−	+	+	+	+
−	−	−	+	−	−	−	−
131 lb. 136 lb.	134 lb. 131 lb.	131 lb. 130 lb.	140 lb. 136 lb.	98 lb. 94 lb.	140 lb. 132 lb.	147 lb. 121 lb.	136 lb. 134 lb.
120/75	150/70	140/70	126/70	130/85	128/68	122/78	125/76
125/75	165/60	136/72	124/75	136/90	130/70	100/60	128/75
32 days	24 days	53 days	67 days	18 days	18 days	20 days	45 days
1,200 r	1,200 r	1,550 r	2,000 r	1,400 r	1,200 r	300 r	1,800 r
0.88	0.35	1.65	2.81	1.33	1.2	1.1	2.72
1 day 40 mg.	... 10 mg.	1 day 30 mg.	2 days 30 mg.	1 day 30 mg.	... 10 mg.	1 to 2 days 50 mg.	1 day 30 mg.
5 days	1 day	3 days	5 days	4 days	1 day	7 days	3 days
6 days	2 days	3 days	5 days	5 days	2 days	8 days	4 days

possibility that the favorable results subsequently obtained with larger doses might be due solely to a psychological effect. The dose was therefore doubled, and all patients subsequently treated were started on 10 mg. This is one-half to one-fourth of the minimum amount used by Massell and Warren (22) in their successful treatment of rheumatic fever and rheumatic carditis, for example. Most of the subjects were treated as out-patients, so that the ACTH (10 mg.) was administered only when they came for their x-ray treatments, daily or thrice weekly. Administration was continued until the symptoms of radiation sickness disappeared. X-ray treat-

ments were never decreased or discontinued during the administration of ACTH. One patient (Case 2) too ill from radiation sickness to come into the office was given her first injection of 10 mg. of ACTH at home and was able to report for treatment the next day. One patient (Case 3) received testosterone for nitrogen balance (23). This was given because of the repeated series of ACTH necessary, and because of the poor physical condition at the beginning of irradiation due to advanced malignant growth. The administration of ACTH was discontinued as soon as the patients were relieved of nausea and vomiting.

CONTRAINDICATIONS TO ACTH

No contraindications to the small doses of ACTH used in these studies have been encountered. It is conceivable, however, that some patients might have an allergic idiosyncrasy, possibly from previous administration of the hormone for some other condition. As pointed out above, ACTH would have little or no value in patients suffering from Addison's disease. Certainly it should be used with great caution in the following conditions, in which the larger doses are usually contraindicated (9): diabetes mellitus, chronic nephritis, hypertension, hirsutism, acne, congestive heart failure, and some mental diseases. It should, of course, never be given to patients with Cushing's disease, which is usually due to an excess of endogenous ACTH (24).

Tuberculosis has been added to the contraindications to ACTH by Emil Bogen of Olive View, Calif., whose work will be published in the Tenth Streptomycin Conference of the Veterans' Administration, 1951. Bogen (25) has shown that ACTH, in doses of one-hundredth the amount usually administered for such conditions as rheumatoid arthritis, activates tuberculosis in as short a time as two weeks, and, therefore, warns against its use in tuberculous patients. He adds that the same may be true of other infections to which one may want to build up an immunity.

Some of the signs of impending danger in the use of ACTH therapy have been reported as side-effects (23): rounding of the face, mild hirsutism, acne, muscular weakness, edema, amenorrhea, red cutaneous striations, and keratosis pilaris. None of these have been seen in the patients treated with these smaller quantities of ACTH for radiation sickness. In fact, no significant change in weight or blood pressure was noted, as shown in Table I.

The following recommendations have been made (23) for the treatment of possible untoward effects of ACTH: low salt and fluid intake for edema; estrogen for rounded facies; potassium chloride (1 gm. t.i.d.) for electrolyte balance; testosterone (25 mg. per day orally) for nitrogen balance, and sedatives for possible psychic phenomena.

RESULTS

All fourteen of our patients were relieved by the 10-mg. intramuscular injections of ACTH daily or thrice weekly while roentgen therapy was continued. Not more than three such injections were required to relieve some of the patients of their radiation illness; and in two (Cases 8 and 12) a single injection sufficed. Two patients required much more than this, although one of these (Case 3) was controlled for two weeks at a time by four or five injections of 10 mg. each of ACTH. The other (Case 5) was finally relieved by a total of 85 mg. of ACTH administered over a period of three weeks, which is less than one-fourth of the amount usually employed in treating chronic rheumatoid arthritis, for example (23). This patient had no function of one kidney and hydronephrosis of the other, due to the extent of her primary disease, which may explain her failure to respond more promptly. One patient (Case 13) died while under treatment. Autopsy revealed widespread lymphosarcoma, which extended laterally beyond the 15×15-cm. ports up the midline.

Table I shows the quantity of ACTH given each patient and the period of such treatment. In none did clinical edema,

rounded facies, psychic phenomena, or electrolyte imbalance develop. Only one (Case 3) needed testosterone for nitrogen imbalance.

LABORATORY FINDINGS

When patients are being treated intensively by the enormous doses of ACTH used in such chronic conditions as rheumatoid arthritis (23), basal metabolic rates are obtained periodically and blood and urine examinations are carried out. Blood counts are made, and sedimentation rates, serum globulin and albumin ratios, serum sodium and potassium, carbon dioxide combining power, fasting blood sugar, inorganic phosphorus, uric acid, urea, creatinine, calcium and free cholesterol are determined. If the fasting blood sugar is elevated, a glucose tolerance test is done. Urine likewise is examined for 17-ketosteroids, 11-oxysteroids, creatinine, uric acid, and glucose in the twenty-four-hour specimen.

In this series, we might expect some of these determinations to be altered due to the primary disease, and others due to the radiation effects. For these reasons, together with the fact that such small doses of ACTH were administered, many of these tests were omitted on most of the patients.

No appreciable changes were found in the excretion studies. There probably were non-detectable physiological and metabolic shifts in those patients whose laboratory findings were not significantly changed following the administration of ACTH. The slight alterations in the 17-ketosteroids and 11-oxysteroids were within the limits of permissible laboratory error and were therefore interpreted as unchanged by the ACTH.

ANIMAL TESTS

After the first 10 patients treated with ACTH for radiation sickness appeared to have benefited thereby, white mice were given total body roentgen irradiation in varying amounts and were then treated with doses of ACTH comparable to those given the human beings, to show that these relatively small doses of ACTH are sufficient to have a real effect.

TABLE II: ANIMAL TESTS

Cage No.	Roentgens*	ACTH†	Mice	Average Length of Life after Irradiation (days)
1	300	Every day	Marked	100 plus‡
		Every other day	Unmarked	11
2	600	Every day	Marked	5
		Every other day	Unmarked	5
3	900	Every day	Marked	3
		Every other day	Unmarked	3
4	1200	Every day	Marked	3
		Every other day	Unmarked	3
5	No	Every day	Marked	100 plus
		Every other day	Unmarked	100 plus
6	300	No		11
7	600	No		3
8	900	No		3
9	1200	No		3
10	No	No		100 plus

* Full dose of total body radiation was delivered at one time with hard x-rays (h.v.l. 4 mm. Cu).

† The daily, or alternate daily, dosage of ACTH was the same per gram of body weight as in a 70-kg. man receiving 10 mg. per day, or every other day, respectively, for ten days starting the day of irradiation. The mice treated daily were "marked," by clipping the ears.

‡ Still living three months after irradiation.

As shown in Table II, 12 mice were exposed to 300, 600, 900, and 1,200 r of hard radiation (h.v.l. 4 mm. Cu). One-third of these were injected daily with ACTH for ten days, beginning the day of exposure. Another third were injected on alternate days for the same period. The remaining third received no ACTH. Control mice which received no irradiation were given ACTH daily or on alternate days, the same as the first two groups of irradiated animals. Other controls were kept under the same conditions of shelter and feeding without having received either irradiation or ACTH.

The results indicate that ACTH administered daily in small doses, 0.15 mg. per kg. of body weight, saves the lives of

mice which have received not more than 300 r of total body irradiation with hard x-rays and prolongs the lives of those exposed to 600 r of total body irradiation, but does not benefit those exposed to still larger doses.

SUMMARY

Fourteen patients were treated for roentgen radiation sickness exclusively with ACTH, receiving 10-mg. injections intramuscularly, daily or thrice weekly while irradiation was continued. Twelve were relieved promptly after a few such injections. In one of these, several relapses occurred, but relief was obtained each time by a few more injections. In the thirteenth patient response was delayed, possibly due to renal complications incident to the primary disease. The fourteenth patient died of his primary disease during this study.

The lives of white mice receiving 300 r of total body roentgen irradiation were saved by daily injections of ACTH for ten days in doses comparable to those given the human beings. ACTH also prolonged the lives of mice which received 600 r of total body irradiation, but it did not benefit those receiving larger doses.

The theory upon which this study was based is discussed. The method of treatment and possible contraindications are given. Reasons for not administering ACTH in sufficiently large doses or for a sufficiently long time to produce untoward side effects are indicated. No valid contraindications to the small doses used in this series were encountered.

The results of the study to date indicate that ACTH in small doses promptly relieves the symptoms of radiation sickness. Further work should be done, however, to prove this conclusively and to evaluate this hormone for the treatment of effects of exposure to fission bomb explosions. Somewhat larger doses of ACTH or its intravenous administration may make it possible to administer radiation therapy more intensively.

ACKNOWLEDGMENTS: Appreciation is hereby expressed to the Santa Ana Community Hospital for initially financing this study and to Mr. Wm. O. Robison, R.T., for the special laboratory procedures performed by him at this Hospital. The help of my technicians, Howard P. Forehan, R.T., Mahlon A. Smith, R.T., Margaret Morris, R.N., Mrs. Beverly A. Booth, R.T., A.S.C.P., James Pursell, and Rebecca Portugal is acknowledged; also the assistance of Mrs. Frances M. White, in preparing the manuscript.

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SUMARIO

Tratamiento con HACT de la Enfermedad por Irradiación. Informe Preliminar sobre Catorce Casos

Catorce sujetos fueron tratados por enfermedad debida a los rayos X exclusivamente con HACT, recibiendo inyecciones intramusculares de 10 mg. diariamente o tres veces semanales mientras continuaba la irradiación. Doce se aliviaron prontamente después de algunas de esas inyecciones. En uno de ellos, ocurrieron varias recidivas, pero se obtuvo alivio cada vez con algunas inyecciones más. En el décimotercer enfermo, se dilató la respuesta, posiblemente debido a complicaciones renales incidentes a la afección primaria. El décimocuarto enfermo falleció de la dolencia primaria durante el estudio.

A ratones blancos que recibieron 300 r de irradiación roentgen total en el cuerpo se les salvó la vida con inyecciones diarias de HACT durante diez días a dosis comparables a las administradas a los seres humanos. La HACT prolongó también la vida a ratones que recibieron 600 r de irradiación orgánica total, pero no benefició a los que recibieron dosis mayores.

El tratamiento con HACT de la enfermedad irradiatoria se basó en la hipótesis de que los síntomás podrían deberse a envenenamiento por productos de la descomposición histológica, parecidos a la histamina, según indicaba el alivio obtenido en el pasado con drogas antihistamínicas. El A. no observó efectos adversos después de las pequeñas dosis de HACT empleadas en esta serie, pero no hay que dejar de tomar en cuenta las habituales contraindicaciones al empleo de la droga en mayores cantidades.

Backache and Its Relation to Ruptures of the Intravertebral Disks[1]

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DISK PROTRUSION was first described in 1857 by Virchow, who mentioned a cervical "ecchondrosis" with lethal compression of the spinal cord. The first description of disk rupture came one year later in a monograph by Luschka, called *Die Halbgelenke des menschlichen Körpers.* Actually, however, there are drawings of ruptured disks in two earlier textbooks of anatomy: Weitbrecht's *Anatomie* of 1742 and Henle's *Bänderlehre* of 1856; these drawings were made to illustrate the normal anatomy of the intervertebral disk, since the pathological condition was not recognized at that time.

More and more has gradually been added to our knowledge of disk rupture and its clinical importance. The greatest step forward was made by American neurosurgeons, who proved at operation that disk prolapse not only might cause but actually was a common cause of low back and sciatic pain.

Personally, I became interested in this field twelve years ago, when Dr. Love, while in Sweden, demonstrated the surgical treatment of disk prolapse. As a roentgenologist I performed myelography in cases of sciatica, with the same unhappy experience as others: many suspected disk cases appeared normal myelographically, and some with positive myelographic findings appeared normal at operation. I decided then to try to visualize the rupture itself by puncture of the disk and injection of contrast medium into its center.

I began with a roentgenographic-anatomical study of specimens in which the disks were injected with red lead in gelatine, a method which had been used on occasion by Schmorl and Junghanns in their anatomical studies. This proved to be most successful. All ruptures were visualized, even minor ones representing the early stages. A careful dissection of the specimens was made before the disks were cut. The posterior wall of the spinal canal and the intervertebral foramina were removed. The dural sac, with the nerves and the ganglia, was dissected free and lifted out of its bed. Impressions in the roots and nerves were compared with protrusions of the disks and the intervertebral joints. The disks were then transected at the level at which the ruptures were seen in the roentgenograms. The minor ruptures, it was found, usually ran close to the vertebral surfaces of the disks. On section through the mid portion, the appearance was often normal even in cases of rather extensive rupture.

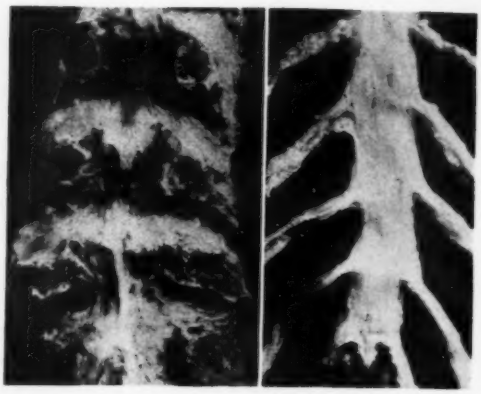


Fig. 1. Photographs of specimen with dorsolateral disk protrusion compressing the fifth right lumbar nerve and ganglion (arrow).

Disk protrusions and herniations, especially into the intervertebral foramina (Fig. 1), proved to be very common and the adjacent nerves and their ganglia were

[1] From the Diagnostic Department of Roentgenology, Karolinska Sjukhuset, Stockholm, Sweden (Chief: Professor Åke Åkerlund). Fifth Annual Leo G. Rigler Lecture in Radiology, University of Minnesota, Nov. 2, 1950. Accepted for publication in March 1951.

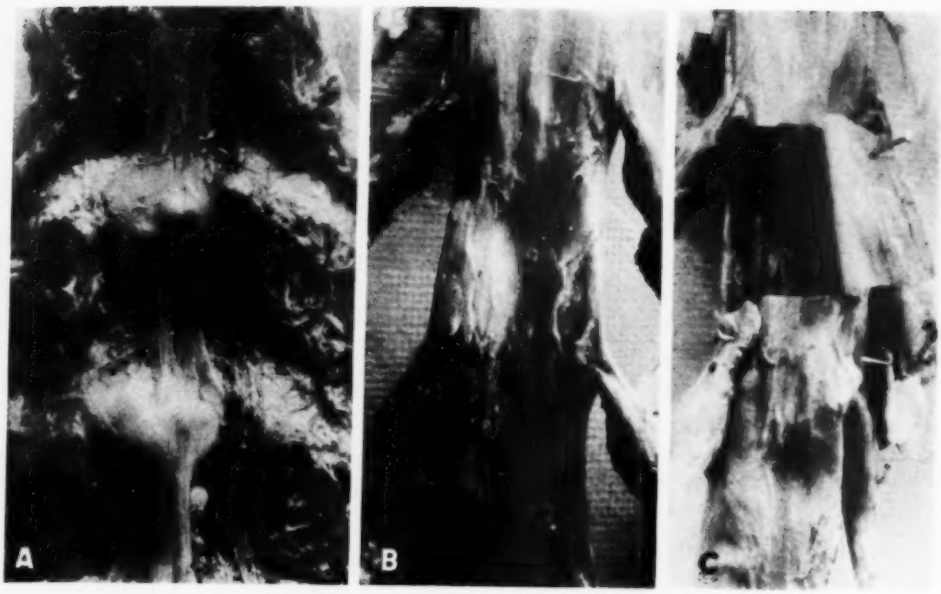


Fig. 2. Photographs of specimen with posterior rupture and bulging of third lumbar disk causing compression of nerve roots (c).

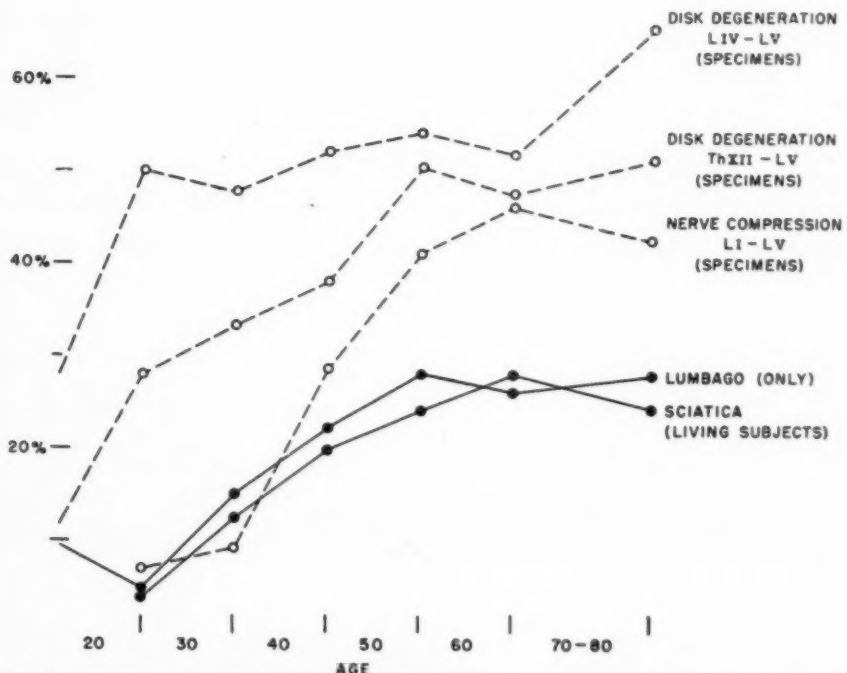


Fig. 3. Occurrence of disk degeneration and nerve compression in autopsy specimens, and lumbago and sciatica in living subjects without actual symptoms.

compressed. A few root compressions by arthritic osteophytes from the intervertebral joints were also found, although always in association with disk rupture. In no case was there hypertrophy of the ligamentum flavum.

Nerve compressions were caused by naked herniations as well as by bulging disk surfaces (Fig. 2) under which there was always a rupture and protrusion of disk substance.

Therefore, we may assume that, with a few exceptions, low back and sciatic pain means disk rupture and protrusion.

EXPERIENCE WITH DISK PUNCTURE

Several years passed between this anatomical study of injected disks and the clinical use of disk puncture. It was necessary to wait for the results in reoperated disk cases in which disks had been punctured or incised at the first operation without positive findings and then failed to demonstrate any protrusion at a second operation. In addition, intervertebral disks in dogs' tails were punctured and injected with diodrast; on removal, later, the tails showed no evidence of damage, no structural changes, and no protrusions.

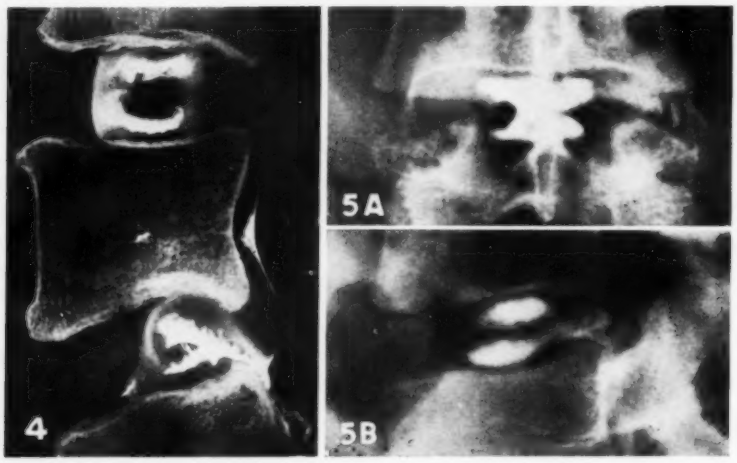


Fig. 4. Discogram in autopsy specimen. Normal L-4; posteriorly ruptured L-5.
Fig. 5. Discograms of L-4 in living subject, demonstrating posterior rupture from the lower disk space.

Serial microscopic sections of compressed nerves and ganglia demonstrated histologic signs of damage to the nervous tissue in the form of degeneration and deformation.

To the anatomical investigation was added a comparative study of the occurrence of nerve compression in autopsy specimens and of low back and sciatic pain in a group of living subjects. This material consisted of patients coming to the hospital for disease other than actual low back and sciatic pain. The comparison showed that there were enough cases of disk rupture and nerve compression in the autopsy material to explain the previous history of low back and sciatic pain which occurred in the living subjects (Fig. 3).

The disk punctures *in vivo* were made with a small needle (0.5 mm. outer diameter). When the needle was inserted into the posterior surface of a normal disk, the patient experienced little or no pain. Posteriorly ruptured disks which later proved to be the cause of low back pain were exquisitely tender—"as if an abscess were being touched," according to the descriptions of some patients.

When the needle reached the disk center,

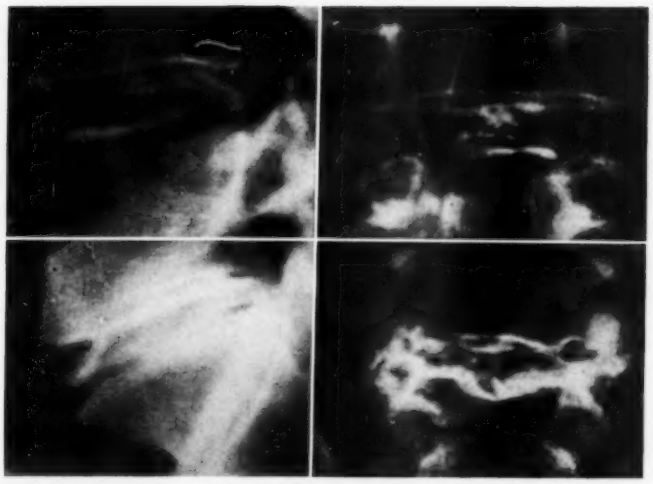
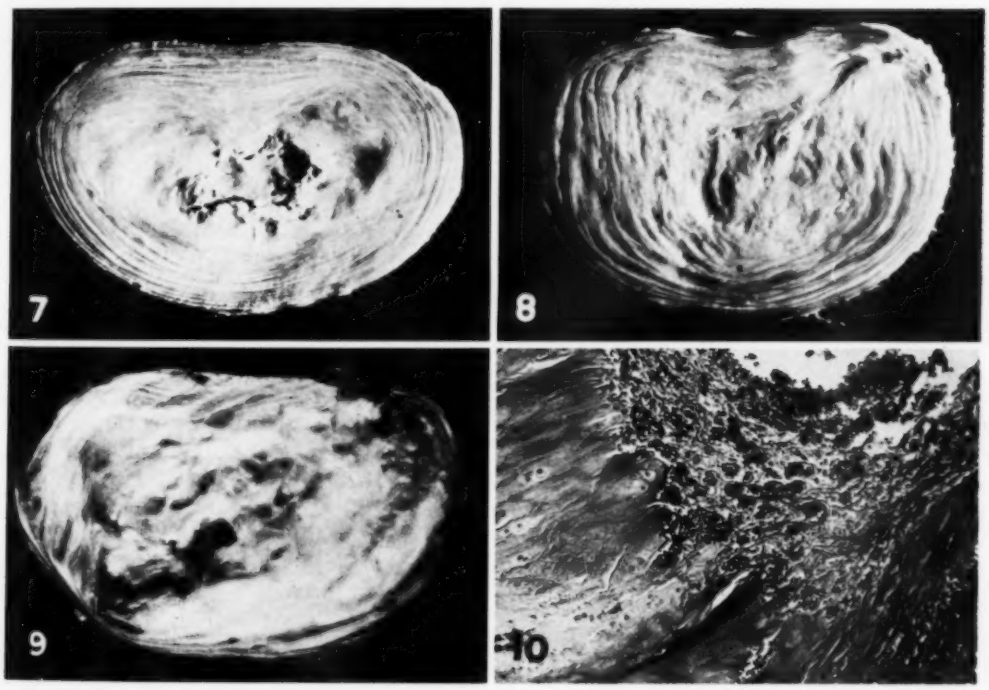
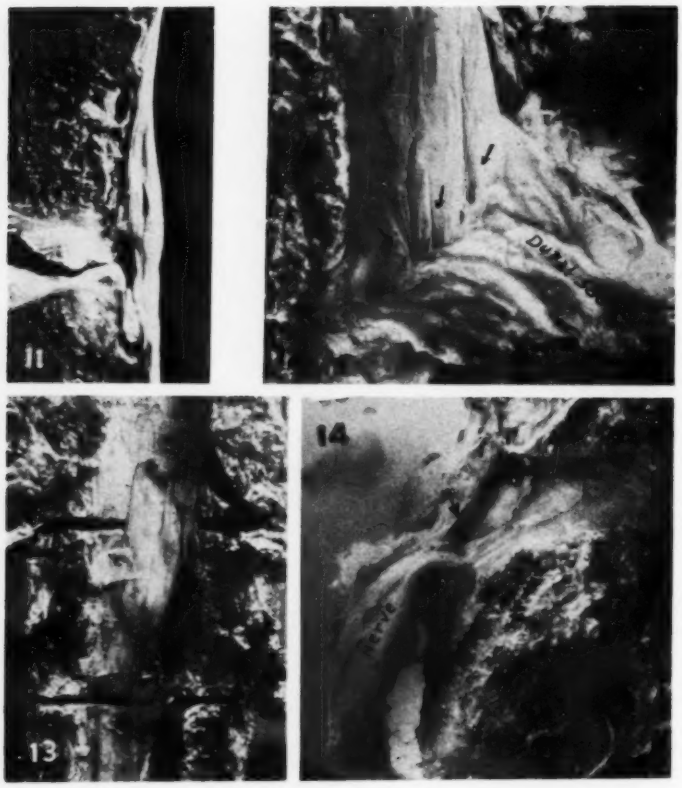


Fig. 6. Discograms of L-4 and L-5 in living subject. More advanced ruptures than in Fig. 5.



Figs. 7-9. Photographs of lumbar disks: normal (Fig. 7); dorsolateral rupture (Fig. 8); final stage with absorbed disk (Fig. 9).

Fig. 10. Photomicrograph of ruptured disk, showing endings of annulus bundles covered with digesting granulation tissue.



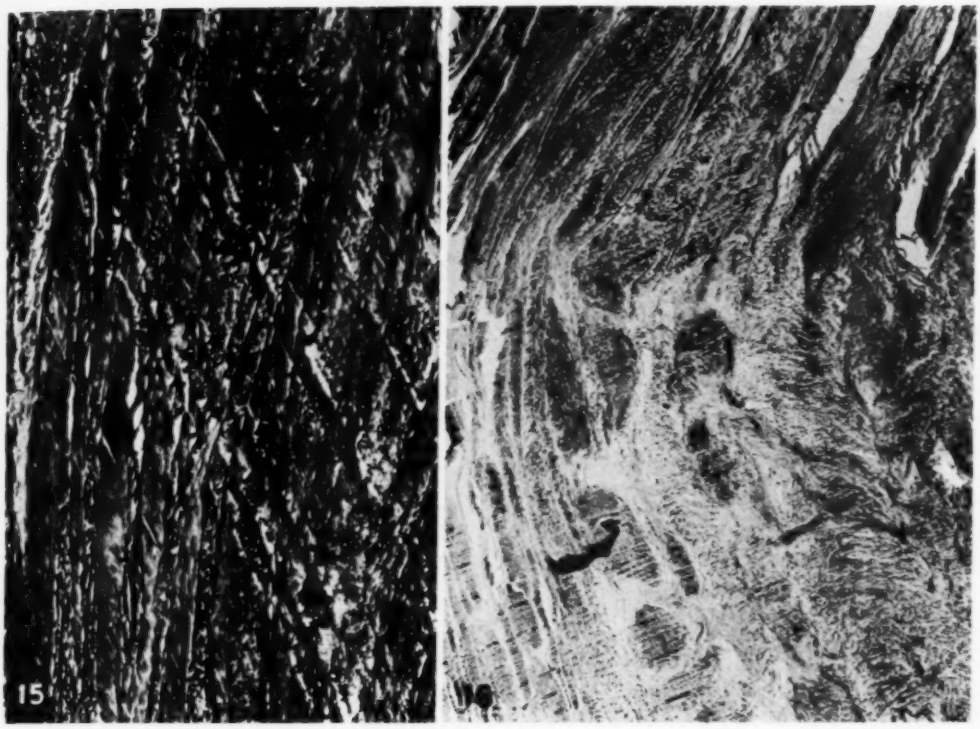
Figs. 11-13. Photographs of autopsy specimens showing posteriorly ruptured disks causing thickening of posterior longitudinal ligament (Figs. 11 and 13) and adhesions (arrows) to dural sac (Fig. 12).

Fig. 14. Photograph of autopsy specimen with dorsolateral rupture and protrusion at L-5 causing adhesions to adjacent nerve (arrow).

a small amount of diodrast with some novocain was injected. The spaces in a normal disk were totally filled by 0.5 c.c.; the distention produced slight back pain at the level of the puncture. Ruptured disks could receive more, and the diodrast leaked out into the surrounding structures through the rupture. The distention of the offending disk by injection either exaggerated or reproduced the low back and sciatic pains.

Immediately after injection, roentgenograms were taken to demonstrate the spaces in the disks and any leakage into the surrounding structures. A normal disk showed the typical two spaces, one cranial and the other caudal to the nucleus pulposus (Fig. 4). Ruptured disks in early stages showed extravasation of the dye through ruptures from one of the two normal spaces (Figs. 4 and 5); the ruptures ran along the adjacent vertebral surface. In more advanced cases the annulus was loosened from the adjacent vertebrae (Fig. 6). Multiple ruptures were common. The diodrast diffused quickly into the disk tissue and was totally gone in at least twenty-four hours.

Until now, in all punctured cases it has been possible to reproduce the low back and sciatic pain, partially or totally. This experience in clinical cases *supports the assumption that low back and sciatic pain, as a rule, are caused by disk rupture. The sharp low back pain seems to originate from posterior ruptures and protrusions in the midline.*



Figs. 15 and 16. Photomicrographs of annulus fibrosus: normal (Fig. 15); normal structure partially replaced by irregular bundles (Fig. 16).

COURSE OF DISK RUPTURE

In anatomical specimens the normal disk had a continuous thick capsule formed by the annulus fibrosus around the nucleus pulposus (Fig. 7). In cases of small radial ruptures the volume of the disk was not decreased and there was no marked loss of nucleus (Fig. 8). In the later stages the volume of the disk was diminished, with prolapse of nucleus and adjacent annulus through broad ruptures up to and sometimes even perforating the surface of the disk. The final stage was a disk consisting almost solely of a thin capsule of the remaining outer layers (Fig. 9).

The protruding tongue of annulus tissue often had a cut-off appearance. Microscopic sections from the tip of these prolapses demonstrated that the endings of the annulus fibers were covered with granulation tissue (Fig. 10). This contained vessels, inflammatory cells, and also giant cells with intracellular remnants of fibrils, probably originating from the digested annulus.

The tissues surrounding a disk protrusion were often sclerosed. The adjacent fat tissue had disappeared and was replaced by a firm connective tissue in which the adjacent nerves sometimes were fixed (Fig. 11). The disk surface and the posterior longitudinal ligament were thickened and fixed to the disk (Figs. 12–14). In a few cases, however, the whole process seemed to have taken place under the disk surface (Fig. 9) and in those cases venous sinuses appeared.

Apparently, the course of a disk rupture is as follows: *Through a primarily radial rupture of the annulus fibrosus the disk tissue herniates toward the surface of the disk, where an inflammatory reaction is produced, digesting the herniating mass and involving adjacent structures such as the*

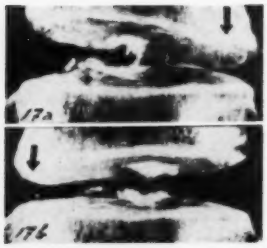


Fig. 17. Discograms of normal disk, illustrating displacement of nucleus by movements of spine. Arrows mark concave side.

posterior longitudinal ligament, roots, ganglia, and nerves. This inflammatory reaction is probably essential in producing pain, as pressure alone on nerves and ligaments is only slightly painful.

The presence of healing at the disk surface was proved by disk puncture. In cases operated upon by incision and curettage it was possible by later puncture and injection to demonstrate that the surgical opening in the disk surface had become obliterated.

PATHOGENESIS OF RUPTURE

The annulus fibrosus in dogs and rats was found to be composed of crossing circular and longitudinal bundles of firm connective tissue with a loose connective tissue between. The same was true of young human specimens. In adults the structure of crossing bundles was still very obvious (Fig. 15). In the posterior parts of the lower lumbar disks, however, it was more common to find this network replaced by more homogeneous fibrous tissue. In the region of an early radial rupture, this homogeneous picture was always present (Fig. 16).

With movements of the back, movement occurs in the annulus (Fig. 17), and conglomeration of its fibrous bundles means that they have decreased individual mobility. This would explain the aforementioned tendency of the annulus to rupture at the insertion into the adjacent vertebrae.

As a disk is vascular only at its surface, most of its nutrition must take place by diffusion. The pumping effect of movements cannot be without value in this respect. Nutrition must therefore suffer from fixation. The above-mentioned conglomeration may be a consequence of such a nutritional disturbance.

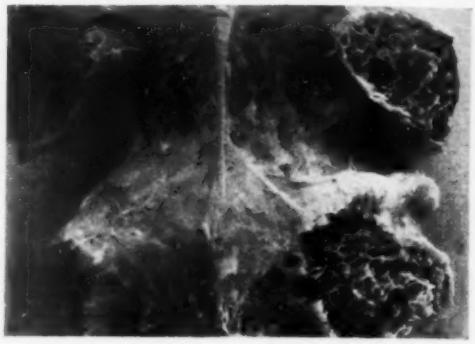


Fig. 18. Photograph of autopsy specimen with sacralized L-5. Protrusion (left) of rudimentary disk.

The intervertebral disk between a sacralized L-5 and sacrum showed a very high percentage of degeneration and rupture. Also osteophytes were found at this site.

Fixation of ankle joints in chickens caused definite changes in the cartilages with loss of chondroitin-sulfuric acid and even synovitis. Fixation of rats' tails in the form of a ring also caused obvious changes in disk structure. In one disk, fixed for five months, a rupture was found on the side of compression (Fig. 19). For definite conclusions on the possibilities of producing disk ruptures by constant compression, more experimental material is needed.

A study of the direction in which radial ruptures tend to occur in anatomical specimens showed a predominance of the posterior and the posterolateral directions in the lower part of the lumbar spine (Fig. 20). It might be possible to explain this by the fact that the spine in modern man is to some degree fixed and posteriorly compressed by his unnatural habit of wearing shoes with heels.

A comparative study was made on 100

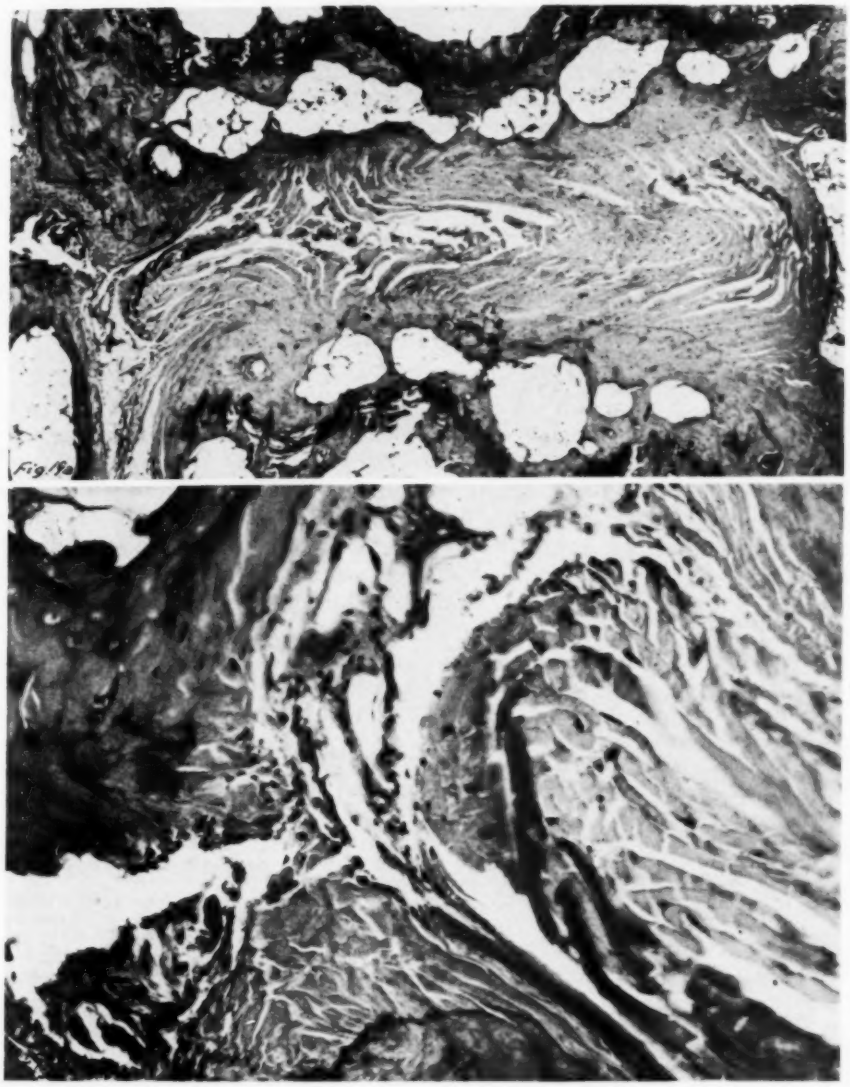


Fig. 19. Photomicrographs of experimental rupture of annulus fibrosus in rat's tail.

prehistoric skeletons and 2,000 roentgenograms from modern inhabitants of Sweden. A definite difference in distribution and degree of marginal osteophytes on the vertebral bodies was found. In the modern material the occurrence of osteophytes was highest at the 5th disk, while in the prehistoric skeletons osteophytes were found predominantly in the mid lumbar region. In skeletons of American Indians and Eskimos the distribution of osteophytes was similar to that in the prehistoric Swedish skeletons (Fig. 21.).

As osteophytes on the vertebral margins almost never occur without disk rupture, their distribution indicates the distribution of ruptures. Some factor in our modern way of living seems to have in-

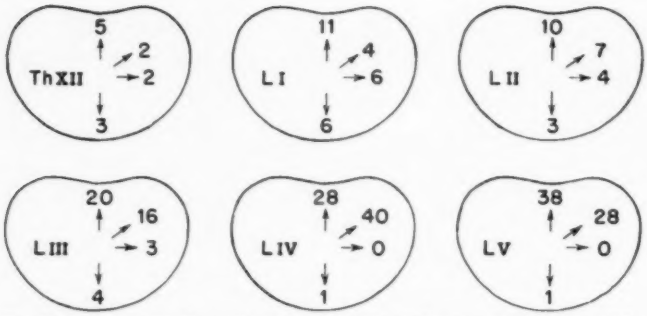


Fig. 20. Diagrams illustrating direction of radial ruptures of lumbar disks in autopsy specimens; number of ruptures as per cent of whole material.

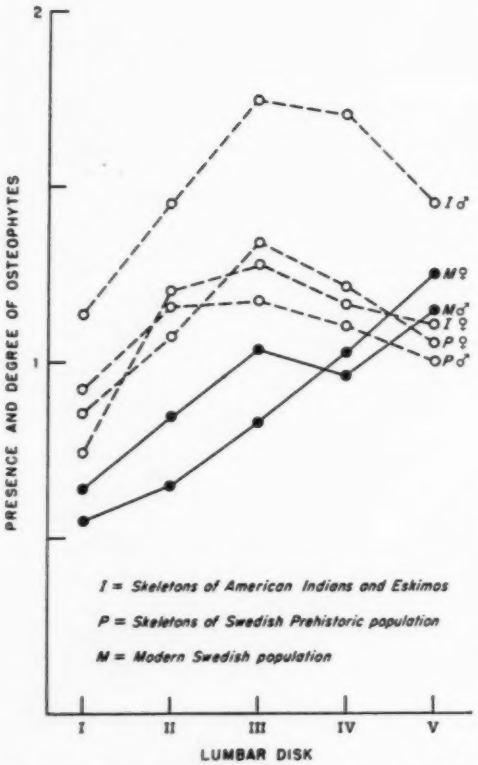


Fig. 21. Occurrence and degree of marginal osteophytes (see text).

creased the tendency of the intervertebral disks to rupture in the lower lumbar region.

Many facts speak in favor of a mechanical factor in the degeneration and rupture of the intervertebral disks. However, it seems obvious that this is only one approach. The problem of disk degeneration and rupture is a part of the problem of aging of the connective tissue in the body.

A huge field is open for further investigation with an inspiring view in prospect—the prevention of disk degeneration and disk rupture, or prevention of backache and sciatica.

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SUMARIO

La Raquialgia y su Relación con las Roturas de los Discos Intervertebrales

Partiendo de las observaciones anatómicas y estudios comparados de la ocurrencia de compresión de los nervios en ejemplares autópsicos y de algias en las regiones lumbar y ciática, el A. deduce que, con pocas excepciones, el dolor lumbar y ciático denota rotura y protrusión de los discos intervertebrales.

Apoyan además esta opinión los resultados de la punción de los discos y la introducción de diodrasto en los espacios de los mismos. La distensión de un disco roto por el medio inyectado bien exageró o reprodujo el dolor.

La evolución de la rotura de un disco parece ser así: A través de una rotura primordialmente radial del anillo fibroso, el tejido del disco se hernia hacia la superficie de éste, en la que provoca una reacción inflamatoria, digiriendo la masa herniada y afectando los tejidos adyacentes, tales como el ligamento longitudinal posterior, las raíces, ganglios y nervios. Esa reacción inflamatoria es probablemente indispensable para la algogenia, pues por sí sola, la compresión de los nervios y ligamentos no produce mas que leve dolor.

Discutida la patogenia de la degeneración y rotura de los discos, dedúcese que muchos datos militan en pro de un factor mecánico. Este, sin embargo, no constituye más que una fase. La situación sólo representa parte del problema del envejecimiento del tejido conjuntivo.

Studies with Radioiodine[1]

III. Problem of Dosage in the Treatment of Hyperthyroidism

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THE AIM OF RADIOIODINE therapy in hyperthyroidism is to produce remission of the disease by adequate irradiation of the abnormal thyroid. The dose delivered by an ionizing radiation to a tissue or organ is best designated in terms of the amount of ionization produced. It would be useful in treatment of the thyroid with I^{131} if the quantity of radiation to which the gland is subjected could be so described.

The dose in millicuries of orally administered I^{131} does not bear a constant relationship to the thyroid radiation dose. Statement of dose in terms of millicuries of I^{131} administered is reminiscent of the early attempts to state therapeutic roentgen dosage in terms of instrument factors and time. In radium therapy dosage is still frequently expressed by the amount of radium used, the filtration, the anatomical position, and the exposure time, rather than in tissue gamma roentgens. Roentgenologists and physicists have developed sufficient understanding and adequate apparatus to permit the statement of the x-ray dose in terms of radiation units in the target tissue. Radium doses are now being defined in a similar fashion by progressive radiation therapists. It seems reasonable to attempt to place I^{131} therapy for hyperthyroidism on a similar radiation-delivered basis. This paper will deal with the evolution of our thinking and experience in attempting to accomplish that purpose.

When this study was initiated, at the end of the Second World War, a few small doses (250 microcuries) of I^{131} were administered weekly for the treatment of hyperthyroidism. This amount was selected because the supply of the isotope was short, and because the evidence then available indicated that such a dose would be safe and yet might be effective. Even then there was reason to believe that this dose was too conservative, since some years earlier Dr. Mayo Soley and others had administered as much as 1 millicurie at one time. However, in the interest of safety, we started the first few patients with one-fourth that amount and observed the effects. Not only did it soon become apparent that no catastrophic events followed the administration of such an amount of radioiodine, but actually little or no effect was observed. The treatment schedule was accordingly revised upward so that the initial doses were on the order of 1 to 2 millicuries. Definite responses were then obtained. In some cases a single dose of this size produced a satisfactory remission of hyperthyroidism, though most patients required several doses. Eventually two selected patients with large goiters were given 4 millicuries as an initial dose without untoward effect.

At this stage reliable apparatus for measuring the radiation from I^{131} had become available. Standardization of the apparatus and studies of the effect of filtration, distance, and size of source on the measurement of gamma rays from radioiodine permitted a reasonably accurate determination of its amount in the thyroid. The work of Marinelli and Quimby (1, 2) which had to do with the calculation, in roentgen equivalent physical units (rep), of the radiation dose delivered to a

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tissue by a radioactive isotope came into our thinking.

It was now possible to administer a dose of I^{131} to a patient and to determine the amount in the thyroid at any time thereafter. Assuming uniform distribution of a radioactive isotope, knowledge of the amount of the isotope present in a tissue as a function of time, and the weight of the tissue, permits a calculation of the radiation dose in rep. (A discussion of this calculation is presented in the Appendix.) In the early I^{131} uptake studies it had been observed that, if the first of two successive doses given to a patient was small, and the interval between doses short, the two thyroid uptake curves were similar. This seemed to be true regardless of the size of the second dose. In terms of per cent of the amount administered, the uptake maxima for two such doses reached roughly the same value. It thus seemed possible to use the I^{131} uptake data obtained from the administration of a preliminary test dose to estimate the amount that would have to be administered to give any desired amount of radiation to the gland.

As referred to hereafter, a test dose is a small initial dose of I^{131} (100 microcuries or less) administered for the purpose of determining the thyroid uptake curve, *i.e.*, the per cent of the administered dose present in the thyroid as a function of time. The therapy dose is that given to the patient for the purpose of treating his disease. The "preselected" radiation therapy dose is the number of β-rep that one intends to give to the thyroid by the therapy dose. This value can be translated into millicuries of orally administered I^{131} by the methods described in the Appendix. The "actual" radiation therapy dose is the number of β-rep delivered to the thyroid by the therapy dose as determined by the uptake curve of that dose and the use of the method described in the Appendix.

Only patients with definite hyperthyroidism were accepted for treatment. Patients with nodular goiters were excluded from the series because of lack of homogeneity in the distribution of the iodine in thyroids thus affected. Each patient of the first series was given a "preselected" therapeutic dose of 3,000 β-rep. No remissions were achieved, however, and the "preselected" dose was consequently raised to 4,000 β-rep. Although some response was obtained with this dose, it was still too small. Finally, it was raised to 6,000 β-rep. At this level most of the patients were markedly improved on the first dose, and some even appeared to be cured. While it is true that many patients required more than one treatment, the response to an initial "preselected" therapy dose of 6,000 β-rep was so satisfactory that its use was continued.

In each case the uptake curve of the therapy dose was determined. In this way the "actual" β-rep dose delivered to the thyroid by the therapeutic dose could be calculated and compared with the "preselected" dose. Since each uptake curve required observations over a period of five to seven days, the procedure was time-consuming and expensive, but, in retrospect, it enabled us to determine how closely the values for the "preselected" and the "actual" therapeutic doses agreed. It became apparent that there were indeed some large discrepancies between the doses that were planned for a patient and the amount of radiation "actually" received.

Forty-three hyperthyroid patients, previously untreated with radioiodine, were given amounts of I^{131} intended to yield 6,000 β-rep, and the "actual" therapeutic dose was calculated. As shown in Figure 1, there was frequently a wide variation between the "preselected" and the "actual" dose of radiation delivered to the thyroid. In reviewing the test and therapeutic dose uptake curves for this group, it was found that the values for maximum uptake and the effective half-life of the isotope often differed between the two curves for a given patient. These variations seemed too great to be accounted for by inaccuracies of measurement; it seemed more likely that they were due to changes in the iodine avidity of the active thyroid tissue.

It should be emphasized that there were

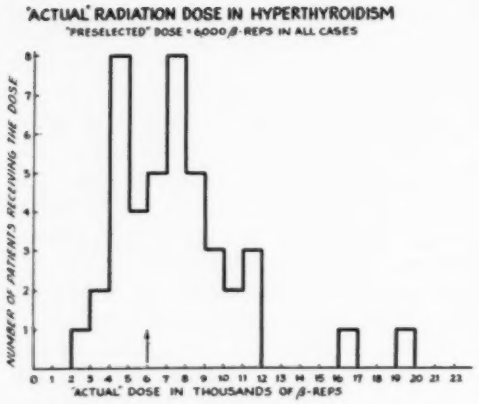

Fig. 1. Comparison of "preselected" and "actual" doses of radiation from I^{131} in 43 patients with hyperthyroidism. None of these patients had previously been treated with radioiodine. Each had received a small test dose of I^{131} about one week before the administration of the therapy dose.

The "preselected" dose in each case was 6,000 β-rep. The "actual" doses show a considerable range of values.

no detectable changes in thyroid weight between the test and therapy doses. While it is recognized that there are errors in judging thyroid weight, such an error would be equally reflected in the calculations of the "preselected" and "actual" dose and consequently will not explain the discrepancies between the two. Whatever the explanation, it is apparent that, since the β-rep value is proportional to the product of maximum uptake and effective half-life, changes in such uptake and half-life will be reflected in this value. Figure 2 shows the percentage difference between the product of maximum uptake and effective half-life for the test dose and for the therapy dose for 38 patients in whom adequate data were available. The distribution and range of the data are similar to those in Figure 1 and do explain the differences found between the "preselected" and the "actual" radiation therapy doses. The data for Figure 2 are from patients receiving their first I^{131} studies and treatment. The data from subsequent studies of these and other patients are consistent with the above results but are not included in this report, since it seemed better to limit the comparison to patients not previously treated with I^{131}. While the method

TABLE I: RESPONSE OF 38 HYPERTHYROID PATIENTS TO INITIAL "ACTUAL" RADIATION THERAPY DOSE

"Actual" Initial Dose β-rep	Became Euthyroid	Remained Hyperthyroid	Became Hypothyroid
2,500–4,500	1	5	1
5,000–7,000	4	6	0
7,500–9,500	5	6	3
10,000–12,000	1	2	2
Above 12,500	2	0	0

we were applying appeared to be based on rational grounds and our aim was to treat hyperthyroidism with I^{131} in such manner that the amount given was determined by the ionization desired in the tissue, the method did not yield data that would permit us to predetermine the dose with enough accuracy to make the effort seem worth while.

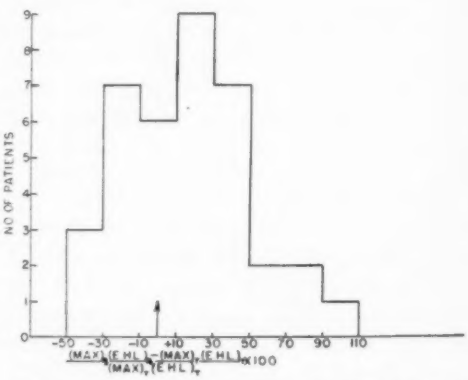

Fig. 2. Percentage difference between the product of the maximum uptake and the effective half-life of the initial test dose and of the initial therapy dose in 38 patients with hyperthyroidism treated with I^{131} for whom adequate data were available. Subscript rx refers to therapy dose and subscript T refers to test dose.

At the onset of this work it was hoped that it would be possible eventually to correlate the radiation dose to the thyroid with the response obtained in the hyperthyroid patient. This would have yielded a numerical value for the amount of ionization desired in the tissue. The data showed that, while most of the patients exhibited a response to the initial therapy dose, the degree of response was not predictable and did not correlate well with the "actual" radiation dose (see Table I).

An extreme example of the lack of cor-

TABLE II: STATUS AFTER THE FIRST DOSE OF I^{131} OF 88 OF FIRST 100 HYPERTHYROID PATIENTS TREATED (mc I^{131}/gm. thyroid)

Dose mc./gm.	Euthyroid	Hypothyroid	Still Hyperthyroid
0.000–0.068	0	0	17
0.070–0.089	0	0	6
0.090–0.109	4	0	14
0.110–0.129	5	0	11
0.130–0.149	0	1	9
0.150–0.169	4	1	1
0.170–0.189	6	0	1
>0.190	4	1	3
Total	23	3	62

relation between (*a*) the "preselected" and the "actual" radiation dose, and (*b*) the "actual" dose and response is furnished by one patient who received an initial "actual" dose of over 19,000 β-rep. The "preselected" dose in this case was 6,000 β-rep. This discrepancy between the "preselected" and the "actual" dose occurred because the values of the maximum uptake and the effective half-life were both larger in the therapy dose than they were in the test dose. Since many patients had become euthyroid or even hypothyroid on single or accumulated doses of considerably less than 19,000 β-rep, it was expected that this patient would become rapidly and profoundly myxedematous. To our surprise and relief, he became euthyroid in a few weeks and has remained so (one year).

These experiences indicated that attempts to get at the dose problem in the manner described were not very effective. The end-result did not justify, on other than an experimental basis, the time and work required.

In an endeavor to find another basis for determining a therapeutic dose, the data were re-examined. In the first 100 consecutive hyperthyroid patients treated with I^{131} in this clinic, the records of 88 were regarded as adequate for this purpose. In Table II the responses to the initial therapeutic doses for these 88 patients are shown. Here the dose is given as millicuries of orally administered I^{131} per estimated gram of thyroid tissue; no account is taken of amount of uptake or effective half-life. It is seen that in no case was remission achieved with an initial dose of less than 90 microcuries per gram, that no patient became hypothyroid with an initial dose of less than 130 microcuries per gram, and that in several instances remission occurred with doses between these two levels. Furthermore, of those patients receiving less than 110 microcuries per gram, 90 per cent required further I^{131} therapy.

Table III presents a summary of the final therapeutic results in these same 88 cases. Here again the dose is in oral millicuries per estimated gram of thyroid tissue, representing in this instance a total of all I^{131} received by the patient throughout the course of therapy. It is seen that no patient became euthyroid on less than 78 microcuries per gram;[2] only one did so on less than 90; the majority required more than 130 microcuries per gram; and in no instance was hypothyroidism produced on a total dose of less than 139 microcuries per gram. From these observations, it appeared that, had we arbitrarily selected a dose of 120 microcuries per estimated gram of thyroid tissue initially, the success of the therapy would have been as great as it was with the more complicated method we employed. Furthermore, the incidence of hypothyroidism produced would probably not have been greater.

TABLE III: STATUS OF 88 OF FIRST 100 HYPERTHYROID PATIENTS TREATED (mc I^{131}/gm. thyroid)

Status after Completion of Therapy	Total Dose mc./gm.	Number
Euthyroid	<0.078	0
Euthyroid	0.078	1
Euthyroid	0.090–0.129	13
Euthyroid	0.130–0.677	61
Euthyroid	1.121	1
Hyperthyroid*	0.218–0.633	7
Hypothyroid	<0.139	0
Hypothyroid	0.139–0.209	5

* Operated or lost before completion of therapy.

A series of hyperthyroid patients is now being treated on the basis of 120 microcuries per gram of thyroid tissue. The

[2] In one patient whose initial dose was 80 microcuries per gram, two additional doses brought the total to 78 microcuries per gram and produced euthyroidism.

TABLE IV: RESULTS OF TREATMENT OF 21 HYPERTHYROID PATIENTS WITH I^{131}*: DOSE APPROXIMATELY 120 μC PER ESTIMATED GM. THYROID TREATMENT

No. of doses of I^{131}	1	2	3
Euthyroidism	11	3	1
Improvement, but not euthyroidism	10	5	1
Hypothyroidism	0	0	
Total	21	8	2

* Follow-up time 2 to 10 months only.

Of the 21 patients who were treated by this method, 8 were given a total of 2 doses, and 2 were given a total of 3 doses. Of the 5 who were improved after the administration of 2 doses, some may need a third dose. In no patient did hypothyroidism develop.

series now numbers only 21 patients and the follow-up periods are not yet long enough to permit adequate analysis of the results. This method of treatment has been used by others for a long time with apparent success. We preferred not to accept it as a standard means of therapy until the methods of predetermining dosage in radiation units had been investigated. At the present time, a patient suspected of hyperthyroidism can be seen in the morning, studied clinically, given a diagnostic five-hour I^{131} thyroid uptake rate determination and a basal metabolic rate determination, and, if the diagnosis is accepted as hyperthyroidism, be treated by mid-afternoon of the same day and sent home. So far, the response to this regimen is quite satisfactory (Table IV).

SUMMARY

Since the treatment of hyperthyroidism by radioiodine is essentially radiation therapy of the abnormal thyroid, it would be advantageous if the proper radiation dose to the thyroid could be predetermined and could be expressed in roentgens. This paper deals with attempts to accomplish this. A test dose of I^{131} was given to the patient, the thyroid uptake curve was determined, the thyroid weight estimated, and the amount of I^{131} necessary to give the predetermined dose calculated. When this amount of radioiodine was given to each of a number of patients, it was found that the "preselected" radiation dose as calculated from the test dose uptake curve frequently differed from the "actual" radiation dose as calculated from the uptake curve of the therapeutic dose. These differences were dependent upon changes in effective half-life and maximum uptake between test dose and therapeutic dose.

A study of the results of treatment of hyperthyroidism by I^{131}, with the dose expressed in terms of microcuries per estimated gram of thyroid, showed that some remissions were achieved and that no hypothyroidism was produced by initial doses of 90 to 129 microcuries per gram. Treatment of a series of patients has accordingly been started with 120 microcuries per gram of thyroid as an initial dose. To date this dose of radioiodine seems satisfactory for the first treatment of hyperthyroidism in patients with diffuse toxic (not nodular) goiters. If necessary, subsequent doses of radioiodine are administered, their size being based on the response of the patient to the first dose.

APPENDIX

Calculation of the Radiation Dose Delivered to the Thyroid by I^{131}

In therapy with beta-emitting isotopes it has become conventional to speak of radiation dose to tissue in terms of the beta-roentgen equivalent physical unit (β-rep). A β-rep may be defined as that amount of beta radiation which, under equilibrium conditions, releases in 1 gram of air as much energy as 1 roentgen of gamma rays. Also, a β-rep of beta-particles will deliver to a gram of air the same amount of energy as will a roentgen of x-ray. In the calculations, the following assumptions and approximations are made:

1. The energy absorption per β-rep in a gram of tissue and in a gram of air are equal.

2. All the beta particles emitted by I^{131} in the thyroid are absorbed within the gland.

3. The energy absorption is uniform throughout the thyroid.

4. The local effect from the I^{131} gamma radiation is negligible compared with that from the beta rays and is neglected.

5. The weight of the thyroid and the amount of I^{131} it contains may be determined with accuracy sufficient for the purposes of the calculation.

One roentgen (r) produces 1.62×10^{12} ion pairs per gram of air.

One microcurie of a radioisotope is that amount whose atoms are disintegrating at the rate of 37,000 per sec.

Each beta particle from I^{131} can be considered to have 205,000 electron volts on the average. It requires 32 electron volts (this value is variously quoted from 32 to 32.5) to produce an ion pair.

Each beta particle from I^{131}, therefore, when completely absorbed, will produce on the average 205,000/32 ion pairs. Thus the absorption in 1 gram of tissue of the beta particles from 1 μc of I^{131} will produce in one second a dose of $\frac{37{,}000 \times 205{,}000}{1.62 \times 10^{12} \times 32}$ β-rep. This is true only if the number of microcuries is the *same* at the beginning and at the end of the second under consideration in this calculation. But the term microcurie represents a rate which is dependent upon the number of radioactive atoms that are present. In the tissues, this number is always changing. However, if the change in the number of radioactive atoms is small compared to the total number present, the change in rate is small and for practical purposes the number of microcuries can be considered constant.

It is possible to extend such a solution of the problem of determining the number of β-rep delivered to the thyroid even when the rate is changing appreciably, but in a nearly constant manner, if one uses for the calculation the average number of microcuries present during the time interval under consideration. The uptake curve is a graphical expression of the number of microcuries present in the thyroid at all times. When a portion of this curve is a straight line, the number of microcuries is changing at a constant rate. During the time interval represented by this straight line the average number of microcuries can be used in the calculation of dose for this period. For the condition under which an average number of microcuries can be stated for a given interval, the following is applicable:

An average number of microcuries of I^{131} (μc) acting for a number of seconds (t_1) in a number of grams (gm.) of tissue will give to that tissue a dose of $\frac{\mu c \times t_1}{gm.} \times \frac{37{,}000 \times 205{,}000}{1.62 \times 10^{12} \times 32}$ β-rep during time interval t_1. This formula may be expressed as follows:

(*a*) dose $= \frac{\mu c_1 \times \text{seconds}}{gm.} \times 0.000142$ β-rep when time is in seconds

(*b*) dose $= \frac{\mu c_1 \times \text{hours}}{gm.} \times 0.527$ β-rep when time is in hours

(*c*) dose $= \frac{\mu c_1 \times \text{days}}{gm.} \times 12.6$ β-rep when time is in days

Interestingly, the expression $\mu c \times t$ can be represented by the area under the uptake curve when it is plotted with μc and time as coordinates. The area under a curve can be approximated graphically or can be calculated from the equation of the curve. When a graphical solution is used, the curve is divided into time segments and a rectangle is chosen for each segment such that the area of the rectangle is equal to the area under the curve for its particular time segment. The evaluation of the area of the rectangle provides the product of $\mu c \times t$ as required for the solution of formulae (*a*), (*b*), and (*c*).

It has been observed that the descending portion of the uptake curve is often virtually exponential. When this is true, the equation for this portion of the curve may be formulated and the area under it determined by calculation. For this situation the dose formula becomes

(*d*) dose $= \frac{18 \times \mu c_2 \times \text{EHL}}{gm.}$ β-rep

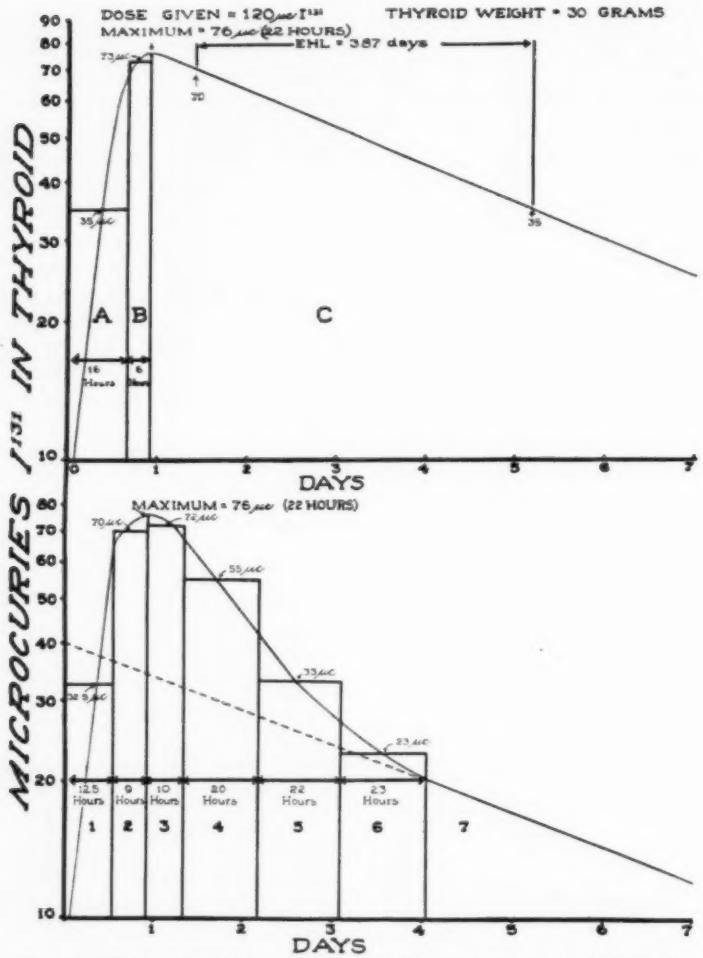

Fig. 3. I^{131} thyroid uptake curves for two different patients. Data from these curves were used to calculate the radiation dose to the thyroid of each patient. It should be noted that, although the oral doses, the thyroid sizes, the maximum uptakes, and the time at which the maxima occurred are the same, one patient's thyroid received much more radiation than the other.

Sample Calculations

Weight of thyroid assumed to be 30 gm. for each example.

Fig. 3 (upper):

$$\text{Part A:}\quad \text{Average } \mu c = \frac{70}{2} = 35. \quad \text{Time} = 16 \text{ hours}$$

$$\text{Dose (A)} = \frac{\mu c \times t}{\text{gm.}} \times 0.527 = \frac{35 \times 16 \times 0.527}{30} = 9.8\ \beta\text{-rep.}$$

$$\text{Part B:}\quad \text{Average } \mu c = 70 + \frac{76-70}{2} = 70 + 3 = 73. \quad \text{Time} = 6 \text{ hours}$$

$$\text{Dose (B)} = \frac{73 \times 6 \times 0.527}{30} = 7.7\ \beta\text{-rep.}$$

Part C: $\mu c_2 = 76$ microcuries. EHL = 3.87 days

$$\text{Dose (C)} = \frac{18 \times \mu c_2 \times \text{EHL}}{\text{gm.}} = \frac{18 \times 76 \times 3.87}{30} = 190.0$$

The total dose is: Dose (A + B + C) = 9.8 + 7.7 + 190.0 = 207.5 β-rep.

Fig. 3 (lower):

$$\text{Dose (1)} \frac{32.5 \times 12.5 \times 0.527}{30} = 7.4\ \beta\text{-rep.}$$

$$\text{Dose (2)} \frac{70 \times 9 \times 0.527}{30} = 11.1\ \beta\text{-rep.}$$

$$\text{Dose (3)} \frac{72 \times 10 \times 0.527}{30} = 12.8\ \beta\text{-rep.}$$

$$\text{Dose (4)} \frac{55 \times 20 \times 0.527}{30} = 19.3\ \beta\text{-rep}$$

$$\text{Dose (5)} \frac{33 \times 22 \times 0.527}{30} = 12.8\ \beta\text{-rep.}$$

$$\text{Dose (6)} \frac{23 \times 23 \times 0.527}{30} = \frac{9.3\ \beta\text{-rep.}}{72.7\ \beta\text{-rep.}}$$

$$\text{Dose (7)} \frac{18 \times 20 \times 4.0}{30} = 48.0\ \beta\text{-rep where } \mu c = 20 \text{ and EHL} = 4.0 \text{ days}$$

The total dose is:

Doses (1 through 6) + Dose (7) = 72.7 + 48.0 = 120.7 β-rep.

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where μc_2 is the number of microcuries present at the beginning of the time for which this part of the calculation is made, EHL is the effective half-life, and gm. is the number of grams of thyroid estimated to be present. The effective half-life, EHL, is the time interval in days between two points on the exponential portion of the curve so chosen that the value for μc at one point is one-half that at the other.

The calculations given above serve as examples of the use of these methods of dose determinations (see Fig. 3). The graphical method of solution is applied to parts A, B, and 1 through 6. In Parts C and 7 the curves have become exponential and formula (*d*) is used. For each curve, addition of the doses determined for the several parts gives the total dose.

It should be noted for the two patients whose uptakes are illustrated in Figure 3 that, although the oral doses, the thyroid sizes, the maximum uptakes, and the time at which the maxima occurred are the same, one patient's thyroid received much more radiation than the other.

Determination of Effective Half-Life

The procedure of determining the EHL is one that takes several days. It would be advantageous, if it were not necessary to determine it for each patient, to use some average value. With this in view, we studied the variation of the EHL in the data from patients with Graves' disease. Figure 4 gives the results of that study and shows the wide spread in the EHL in different patients. Therefore, since the dose of radiation to the thyroid is dependent on the EHL, it is necessary to determine the EHL for each patient when this method of dose calculation is used.

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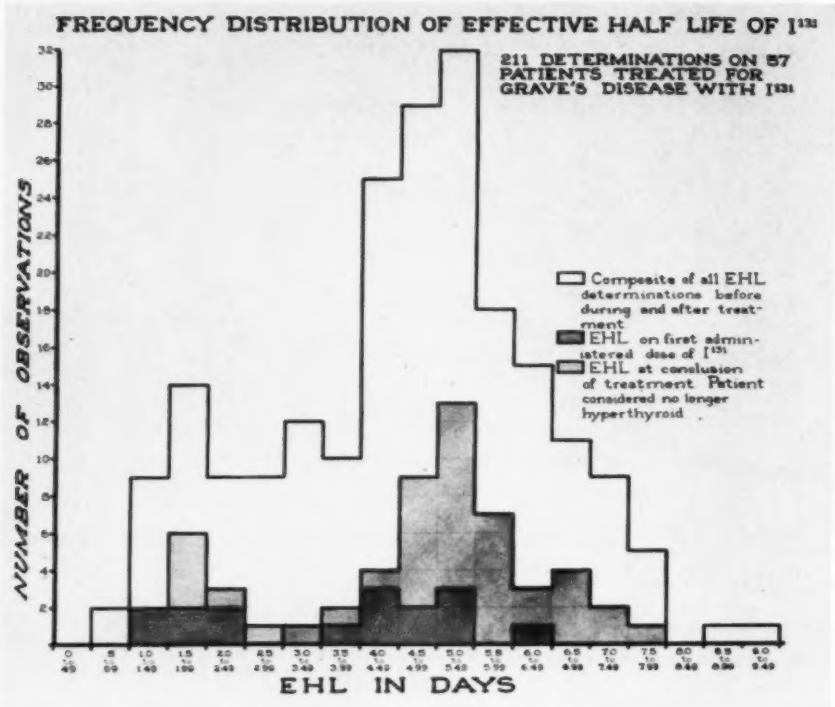

Fig. 4. Wide range of EHL of I^{131} in 211 determinations on 57 hyperthyroid patients. It is apparent that an averaged value of EHL should not be used when calculating radiation dose.

SUMARIO

Estudios con el Radioyodo. III. Problemas de la Dosificación en el Tratamiento del Hipertiroidismo

Visto que el tratamiento del hipertiroidismo con el radioyodo viene a ser en el fondo radioterapia de un tiroides anormal, resultaría ventajoso poder predeterminar y expresar en roentgens la dosis adecuada de radiación para el tiroides. Este trabajo describe esfuerzos emprendidos para lograr esto. Se administró al enfermo una dosis de ensayo de I^{131}, se determinó la curva de absorción en el tiroides, se estimó el peso del tiroides y se calculó la cantidad de I^{131} necesaria para obtener la dosis predeterminada. Al administrar dicha cantidad de radioyodo a cada uno de varios enfermos, se descubrió que la dosis "preescogida" de radiación, calculada por la curva de absorción de la dosis de ensayo, discrepaba frecuentemente de la dosis "real" de radiación, calculada por la curva de absorción de la dosis terapéutica. Esas diferencias procedían de variaciones en la semi-vida efectiva y la absorción máxima entre la dosis de ensayo y la dosis terapéutica.

El estudio de los resultados del tratamiento del hipertiroidismo con I^{131}, con la dosis expresada en microcuries por gramo calculado de tiroides, reveló que se obtuvieron algunas remisiones y que no se producía hipotiroidismo con dosis iniciales de 90 a 129 microcuries por gramo. De acuerdo con esto, se ha empezado el tratamiento de una serie de enfermos con 120 microcuries por gramo de tiroides como dosis inicial. Si parece necesario, se administran dosis subsiguientes de radioyodo, basándose la magnitud de la mismas en la respuesta del enfermo a la primera dosis del isotopo.

Thyroid Carcinoma with Multiple Metastases and Pathological Fracture, Successfully Treated with Radioiodine

Report of a Case[1]

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A CASE OF METASTATIC thyroid cancer is being reported after treatment with radioiodine because of the striking degree of rehabilitation of the patient, the biological effects of a massive cumulative dose on the renal and hemopoietic systems, the interesting histologic radiation changes in the tumor, and the healing of a pathological fracture. This last is of particular interest because of its extreme rarity.

Thyroid carcinoma is relatively rare, contributing only about 0.4 per cent to the total recorded cancer deaths (2). Nevertheless, an intense interest in this entity springs from the fact that a small group of patients with far advanced disease and generalized metastases, particularly to the skeleton, have responded favorably to radioiodine therapy. Although none may be regarded as truly "cured," a few have been maintained in reasonably good health for variable periods up to and beyond the five-year interval.

Conventional treatment of primary thyroid carcinoma involves the use of radical surgery rather than roentgen irradiation or both agents in combination. Prior to the introduction of radioiodine, patients with distant metastases were regarded as completely hopeless. Only a rare "cure" of such a case (by roentgen radiation) has been reported (17). Now such patients who demonstrate a significant uptake of I^{131} by the metastatic foci are treated with that agent, wherever a medical radioisotope team is available.

Unfortunately, not more than 15 per cent of metastatic thyroid carcinoma will pick up radioiodine in amounts that have therapeutic significance (20, 21). Of these cases, about 32 have been described in the literature, and only one-third of this group have benefited by radioiodine therapy.

The metastases of a thyroid carcinoma will not necessarily reflect the same pick-up of radioiodine as the primary lesion. In addition, the metastases may show different degrees of avidity for radioactive iodine in the same patient and in different patients with similar histology (3, 10). Thyroid cancer and its metastases with a good pick-up of radioiodine usually show a mature differentiated histologic appearance approaching that of a normal thyroid (3, 20, 21). However, cellular morphology and cellular function are somewhat independent of each other. A section of thyroid tissue may show excellent differentiation and even colloid formation; yet its radioautograph may demonstrate no pick-up of radioiodine (3–6, 16, 20, 21).

There are several procedures which may be used to stimulate the latent functional capacity of a thyroid carcinoma or its metastases and thus enhance its avidity for iodine, if present or suspected. These have been discussed in the medical literature (9, 11, 13, 14, 16, 18, 19, 20, 22).

In brief, it may be stated that only a small proportion of thyroid cancers, particularly those of slow growth and adenocarcinomatous structure with good morphological differentiation, will approach the iodine-concentrating power of normal thyroid tissue. When the normal thyroid gland is rendered ineffectual by surgery or

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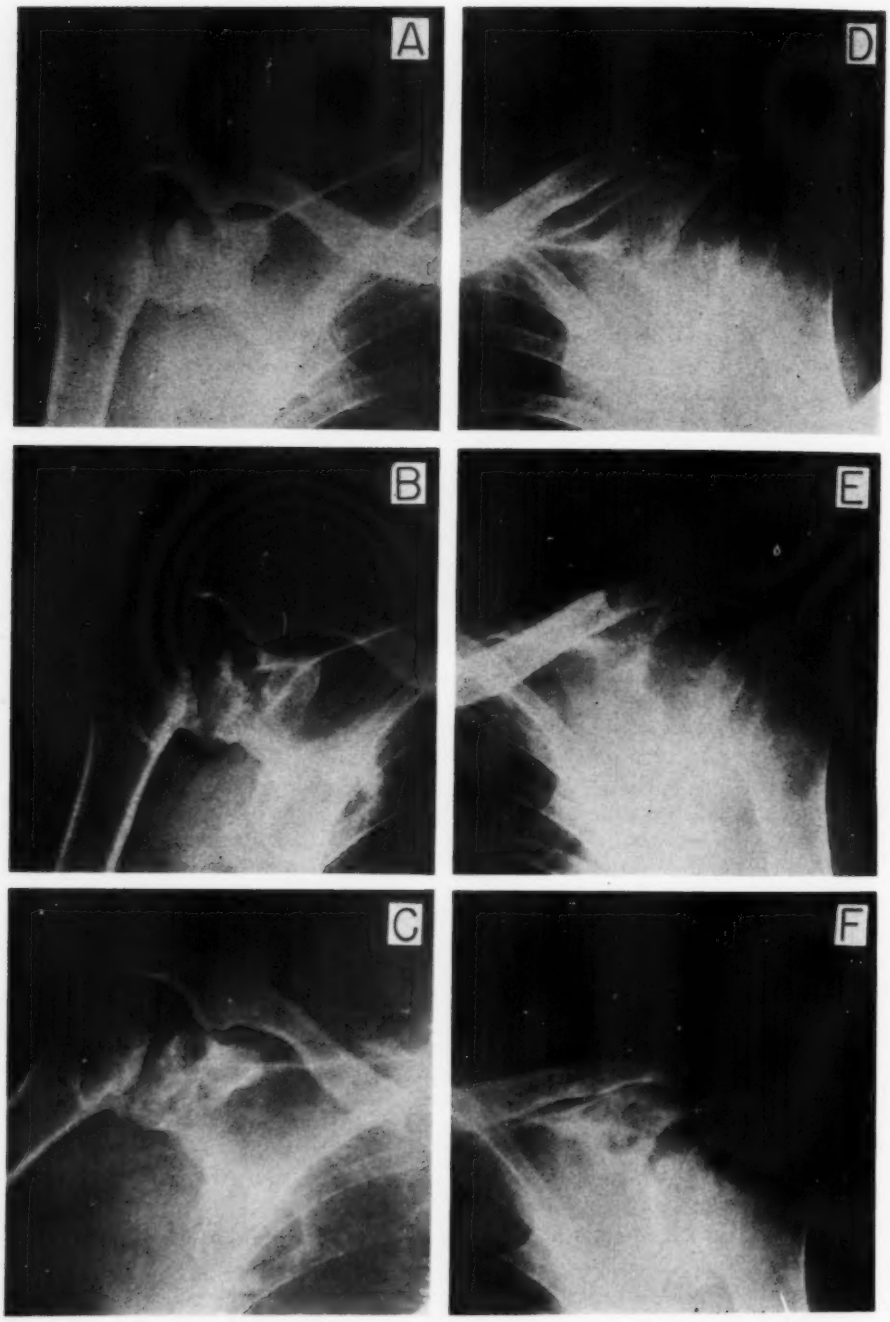

Fig. 1, A. Right shoulder girdle before treatment. Lytic lesion on inferior border of scapula.
B and C. Right shoulder girdle after treatment with I^{131}. Note evidence of progressive healing.
D. Left shoulder girdle before treatment. Complete destruction of the glenoid fossa and neck of the scapula, with soft-tissue mass.
E. Pathological fracture, January 1949, involving spine of left scapula.
F. Left shoulder girdle after treatment with I^{131}. Complete healing of pathological fracture, September 1949, and progressive healing of lesion in glenoid fossa and neck of the scapula.

radioiodine ablation, some of the carcinomatous deposits may concentrate radioiodine or show enhanced concentration and thereby undergo selective irradiation. Such treatment, even though palliative rather than "curative" at present, gives promise of better understanding and possibly control of this type of cancer (15).

CASE REPORT

A 57-year-old white male entered the Veterans Administration Hospital, Bronx, N. Y., in July 1948 because of weakness, marked weight loss, and such excruciating pain in his mid-back that he threatened suicide upon admission to the ward.

In 1933 a subtotal thyroidectomy had been performed in another hospital because of dyspnea secondary to tracheal compression. A mass the size of a grapefruit was removed from the right side of the neck, and a smaller mass from the left side. Unfortunately, the histologic slides and records were lost. In 1942, the left-sided mass recurred and the patient experienced the first of a series of "seizures." During this first "seizure" he was hospitalized elsewhere, with a fracture of the skull and a comminuted fracture through the surgical neck of the right humerus. In 1943 he had a similar "seizure" and was admitted to this hospital for the first time, for observation only. His discharge diagnosis was "fractured skull; fracture through surgical neck of right humerus; recurrent non-toxic goiter of right lobe." Laboratory studies were within normal limits, basal metabolism rate −8 per cent. The "seizures" were controlled with sedative medication and gradually disappeared.

In 1946, because of progressive increase in size of the mass in the right side of the neck, progressive weight loss of 20 pounds, and anorexia, another thyroidectomy was done elsewhere, and the diagnosis of "well differentiated papillary adenocarcinoma of the thyroid with invasion of the veins" was made. Laboratory studies were within normal limits. In 1947, while descending a flight of stairs, the patient toppled and "sprained" his back. Local medication was of no benefit; the back pain became progressively worse and there was continued loss of weight and strength. In January 1948, the family physician obtained a roentgenogram of the spine which revealed destruction of the 12th dorsal vertebra. The patient was hospitalized in April 1948, in another hospital, and received radiation therapy (2,000 r depth dose) to the involved vertebra, with little relief. He became progressively disabled, was unable to walk or work, and was confined to bed.

The second admission to this hospital was in July 1948. The patient appeared chronically ill, with evident weight loss and marked mental depression. The physical findings indicated slight deviation of the trachea to the left and a firm, non-tender mass, about 2 cm. in diameter, palpable at the anterior border of the right sternocleidomastoid muscle, moving with deglutition. A stony hard diffuse mass was adherent to the trachea and also moved with deglutition. A spherical tumor deep in the left pectoral area presented itself over the posterior aspect of the left shoulder. There was a sharp posterior angulation in the lumbodorsal spine, associated with severe pain. Here the overlying skin was pigmented as a result of previous irradiation. The liver and spleen were not palpable. A small lymph node was felt in the right axilla.

Roentgen examination demonstrated no evidence of skull fracture. The chest film (Fig. 2A) showed a deviation of the trachea to the left at the level of the thoracic inlet and deviation to the right just above the aortic arch. The superior mediastinum and the ascending aorta appeared widened. In the lateral view, a mass was observed in the medial aspect of the superior mediastinum. A roentgenogram of the right shoulder (Fig. 1A) showed an old healed fracture of the upper third of the humerus and of the glenoid fossa. Midway along the inferior border of the right scapula was a small expansive lytic lesion. On the left (Fig. 1D) there was complete destruction of the glenoid fossa and neck of the scapula, associated with a soft-tissue mass. X-ray examination of the spine (Figs. 2C and 2E) revealed complete destruction and collapse of the 12th dorsal vertebra, with wedging of its remnants.

After administration of a test dose of radioiodine, a biopsy of the cervical tumor was done in August 1948 and was reported as showing "follicular and papillary carcinoma of the thyroid" (Figs. 3A and 3B). A radioautograph made from this section showed a minimal uptake of radioiodine. Because of the severe back pain, a hyperextension plaster cast was placed about the patient, and some relief was obtained. Laboratory studies showed a normal hemogram, a urinalysis within normal limits on many examinations, basal metabolism rate (Aug. 30) −19 per cent, total cholesterol 250 mg. per cent, blood urea nitrogen 19 mg. per cent. The alkaline and acid phosphatase, blood calcium, and phosphorus readings were normal. The cephalin flocculation test was 2 +, the thymol turbidity −3.

On Aug. 11, 1948, 4 mc. of I^{131} was given orally. The thyroid region then showed an uptake of 21 per cent at the end of twenty-four hours; the twenty-four-hour urinary I^{131} excretion was 56 per cent. The uptake in the metastases could not be shown by *in vivo* Geiger counter studies. A tabulation of all doses and pertinent physical data is given in Table I.

After the first therapeutic dose, the excruciating back pain quickly subsided. On Sept. 13, 1949, both shoulder lesions were biopsied after having received 882 mc. of radioiodine in thirteen months (Figs. 3E, F, G, H, I). These slides show some radiation changes. In January 1949, a painless pathological fracture of the spine of the left scapula occurred (Figure 1E). By Sept. 17, 1949, this was com-

TABLE I: DYNAMIC CHANGES IN LABORATORY FINDINGS

Date	Dose (mc.)	Per cent Uptake, Thyroid Region 24 hr.	48 hr.	Per cent Urine Excretion 24 hr.	48 hr.	Per cent Uptake, L. Shoulder	Biol. H. L. L. Shoulder	Per cent Uptake R. Shoulder	Biol. H. L. R. Shoulder	Remarks
8/11/48	4	21	...	56	68	0	...	0	...	*Radioautograph of primary thyroid cancer showed minimal uptake of I^{131}. No demonstrable uptake in shoulders or spine (9/27/48).
9/27/48	104	14	10	63	85	0	...	0	...	
11/16/48	2	9.5	...	52	75	...	...	...	...	
11/24/48	117	22	10	52	80	6	8	*	*	
1/18/49	1.6	9	...	...	...	...	...	...	...	Mild renal tubular damage; pathological fracture of spine of left scapula (1/18/49).
1/19/49	133	21	7.5	49	49					
2/23/49	2	9								
2/24/49	212			87	88	6	8			
3/10/49	200			76	76					
6/1/49	1	6	3	47						
6/15/49	100	15	8	54	70	6	8	3½	8	
9/13/49	5	11	10	53	73					Both shoulders biopsied (9/13/49). Received 882 mc. I^{131}.
9/23/49	118			40	74	9	8	3½	8	Fracture of spine of left scapula healed (9/23/49).
11/18/49	135	14	8	59	76	8	8	3½	8	Nocturnal leg cramps and impotence (11/18/49).
4/5/50	2	11	8	60	77					Thyroidectomy done (4/18/50).
4/18/50	2									Placed on 1.5 gm. of thiouracil daily for six weeks (5/31/50).
5/31/50	2	7	3	56	76	5		3		Leukopenia due to thiouracil (7/15/50).
7/19/50	2	20	11		49	19	4	6	4	
7/27/50	104	22	6	42	72	10	18	3	30	
	1,246 total dose									

pletely healed (Fig. 1F). The lytic lesions of both shoulders ceased to enlarge and a sclerotic reaction in the surrounding bone developed (Figs. 1B, C, F). The 12th dorsal vertebra remained unchanged, the growth potential apparently arrested by the radioiodine (Figs. 2D, F). No new bony or visceral lesions were observed. Repeated studies during this period showed the basal metabolism rate hovering about −20 per cent. Hemograms were within normal limits. The only change noted was a slight to moderate lymphopenia after each therapeutic dose and a labile platelet count. In January 1949, a 3-plus pitting edema of the feet and ankles was observed. A thorough renal study revealed "mild tubular damage of the kidneys, apparently due to radioiodine." The cardiovascular findings were within normal limits.

In order to increase the retention of radioiodine by the metastases, the patient was placed on thiouracil, 1.5 gm. per day, in May 1950. At the end of one month, administration of the drug was stopped and the patient received a tracer dose of I^{131}. Inasmuch as the uptake in the metastases had not increased significantly, no therapy was given at this time. The patient was continued on thiouracil, receiving 0.5 gm. three times daily for six more weeks. During this period his leukocyte count fell from 6,000 to 3,500. Thiouracil was therefore discontinued. However, since a tracer dose indicated at least a twofold increase in iodine retention by the metastases, the patient was given a 104 mc. therapeutic dose. This dose produced a transitory lymphopenia but there was no aggravation of the leukopenia.

On April 19, 1950, the thyroid region was explored surgically. "On the right side of the neck, the tissues were markedly adherent and replaced by a mixture of scar tissue and cords of tumor. The internal jugular vein and the entire carotid sheath were involved in this process. The parathyroids could not be identified. On the left side only a small piece of tissue could be recognized as thyroid tissue. There was considerably less scarring on the left side." The tissue removed from the right side showed marked histologic changes due to irradiation (Figs. 3C, D, and E). A radioautograph showed a diffuse pick-up by the more cellular portions of the tumor. The area with colloid formation showed no uptake of radioiodine (Figs. 3J, K, and L).

Since the introduction of radioiodine therapy, the patient has become entirely free of pain, walks without difficulty, and has gained 25 pounds. He has returned to normal activity at his occupation as an advertising executive.

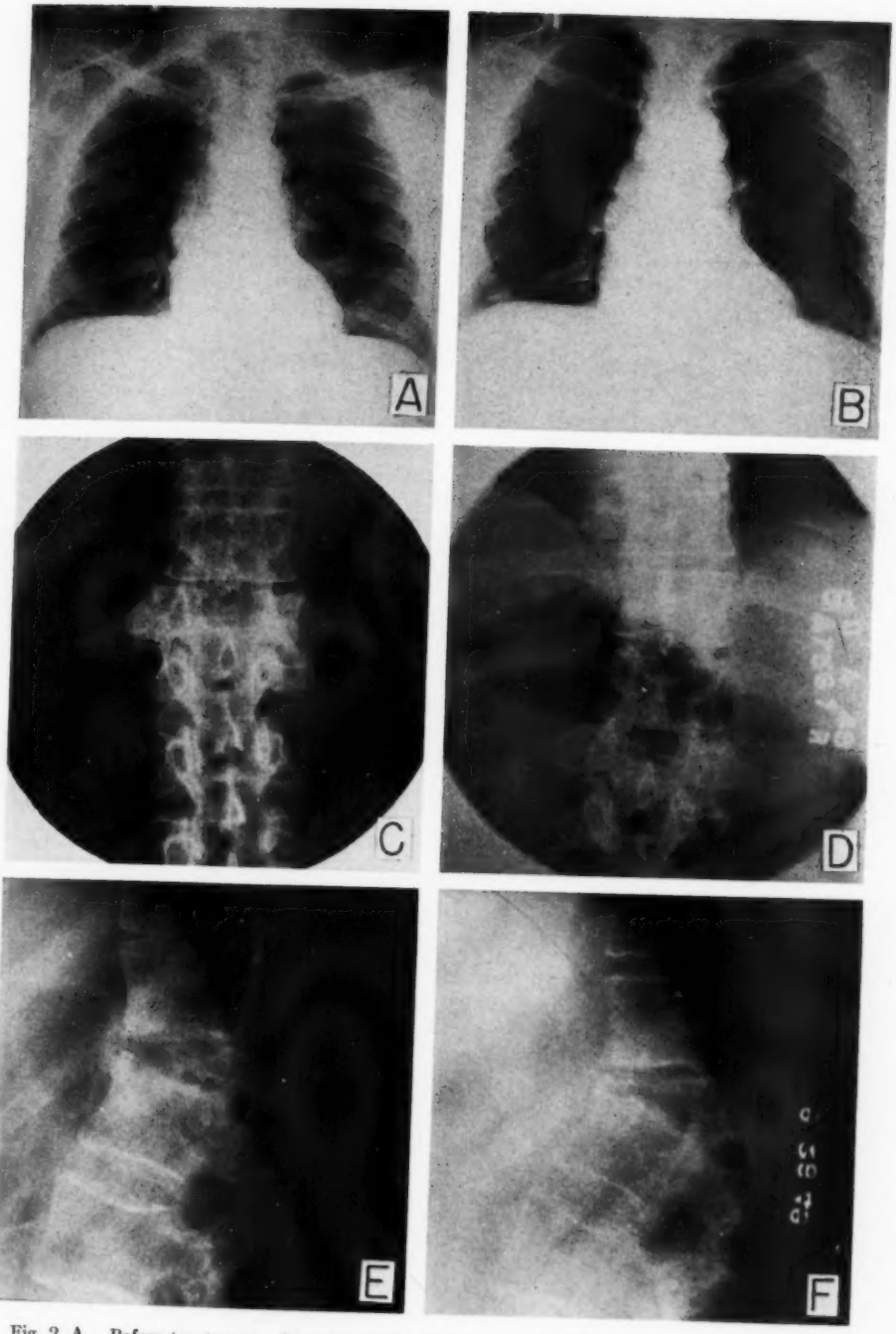

Fig. 2, A. Before treatment. Superior mediastinal mass and deviation of trachea.
B. After treatment with I^{131}. Regression of superior mediastinal tumor.
C and E. Before treatment. Destruction and collapse of twelfth dorsal vertebra with wedging of remnants.
D and F. After treatment with I^{131}. Arrest of the destructive process and development of osteophytes in adjoining vertebrae.

DISCUSSION

This patient has a well differentiated follicular adenocarcinoma with some papillary features. The metastasis in the left shoulder consistently showed an uptake of radioiodine of about 6 per cent of the administered dose in twenty-four hours until the administration of thiouracil. Its volume initially was approximately 500 c.c. (shaped as a truncated pyramid). The metastasis in the right scapula showed an uptake of 3.5 per cent (a sphere 4 cm. in diameter, initially). Both lesions grew, despite radioiodine, for the first three or four months, until the left shoulder lesion was about 800 c.c. in volume, and the right scapular lesion 6 cm. in diameter. In this period the outer third of the spine of the left scapula underwent a painless pathological fracture and during therapy healed in about nine months. Thereafter the lesions showed no additional change, while the surrounding normal bone walled off the lytic lesion by laying down sclerotic bone. In the left shoulder, amorphous calcification appeared in the lytic area to a limited degree. The 12th vertebra has shown no further progressive destruction or collapse, while the development of osteophytes is noted in the adjacent vertebrae. The superior mediastinum, which was widened on admission, has returned to normal appearance (Fig. 2B). The subjective response of the patient has been remarkable in the face of minimal objective evidence of healing.

This patient has received a cumulative total dose of 1,246 mc. of radioactive iodine (I^{131}) in a period of two years. The hemogram has been essentially unaltered except for a transitory lymphopenia and a labile platelet count which is evident twenty-four to ninety-six hours after the therapeutic dose. The renal tubules apparently have been damaged, but not severely. Midway in his therapeutic regime the patient complained of impotence, but refused a testicular biopsy as well as a sperm count. Since then his impotence has disappeared. During the latter phase of his therapeutic period, he has had frequent episodes of leg muscle spasm. An investigation of parathyroid function showed it to be within normal limits.

A most interesting observation has been the marked histologic changes due to irradiation by I^{131}. These changes have been described in the literature (6, 7, 8, 12, 20, and 21), and are adequately demonstrated in Figures 3C, D, and E, and to a lesser extent by Figures 3F, G, H, and I. They consist of cell death, manifested chiefly by lysis of the nucleus and cytoplasm, and to a lesser extent pyknosis and karyorrhexis of the nucleus. Another characteristic cell change produced by the irradiation is the progressive and striking enlargement of the tumor cells, noted in Figures 3C, D, and E. The radiosensitive cells undergo acute cell death but those less radiosensitive show progressive enlargement.

There have been described two types of giant tumor cells. In one variety the cytoplasm shows diffuse, expansive swelling and the formation of degenerative vacuoles of all sizes. The cytoplasm stains palely as though diluted with fluid (Figs. 3C and D). As the cell progressively enlarges, it ruptures and debris is produced as shown in Figures 3E and H. Vacuolation may also occur in the nucleus. The second type of giant tumor cell is due to nuclear changes. Abnormal nuclear forms also occur. Variations in size, shape, and hyperchromatism, which are more characteristic of cancerous change, become accentuated under irradiation (Figs. 3C, D, and E). The hyperchromatic nuclei enlarge and become bizarre until karyorrhexis and karyolysis occur. Other nuclei enlarge and become hypochromatic and finally dissolve. In other cells multiple nuclei develop. Some cells undergo a degree of differentiation, so that in a thyroid cancer Hürthle cells may make their appearance.

The ultimate changes are stromal. These stromal changes appear to be reactive phenomena secondary to the destruction of neoplastic cells. One encounters replacement fibrosis and maturation of

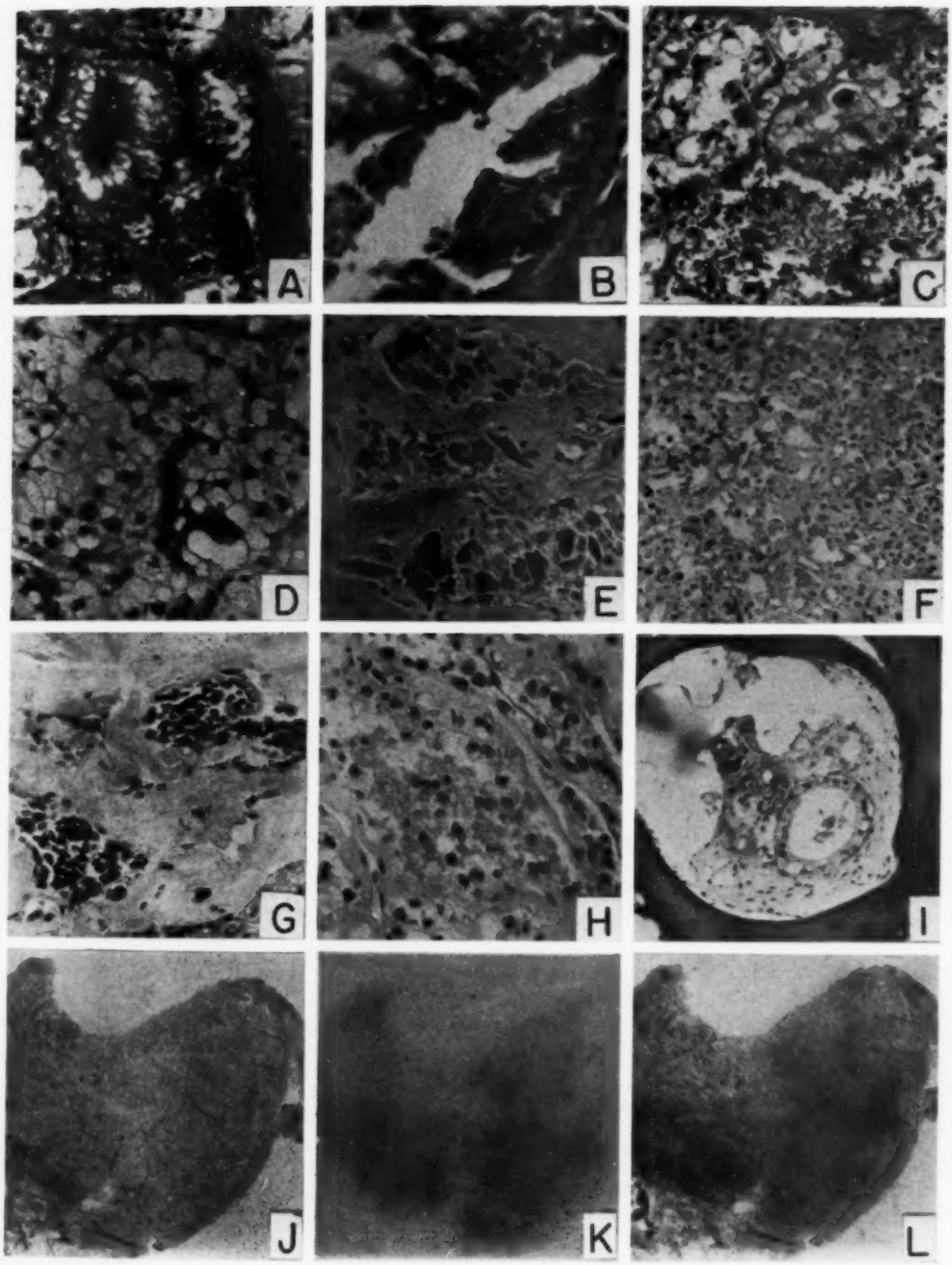

Fig. 3, A and B. Original biopsy of cervical lymph node showing "follicular and papillary carcinoma of the thyroid."

C–I. Serial biopsies of tumor during I^{131} therapy (cumulative dose 1,246 mc.). Note progressive and severe radiation changes in cells and stroma, including pyknosis, karyorrhexis, giant-cell formation, cell destruction, disorganization of alveoli, fibrosis, and hyalinization. Similar changes noted in bone section (I).

J–L. Radioautographs of tumor showing diffuse pickup by the more cellular portions.

connective-tissue fibers. Encirclement of tumor cells and overdevelopment and hyalinization of connective tissue are seen in Figures 3E and G. In the thyroid itself the alveoli become disorganized, the epithelium is transformed into debris, and the colloid is fragmented.

The integral dose was calculated for each therapeutic dose. The calculations are based on those described by F. Bush (1). After each dose blood samples were withdrawn and their activity measured. A curve was plotted over a period of several days. It was noted, as therapy proceeded, that the fraction of the administered dose per gram of blood increased. The circulating radioiodine was highest one to four hours after ingestion of the dose. It usually decreased rapidly and, corrected for radioactive decay, reached a constant value about four days later. Blood samples were drawn until this constancy was established. An eight-day half-life was assumed for this residual activity. An upper limit for the integral body dose was then calculated, on the assumption that the tissues in the trunk of the body contained the same concentration of radioiodine as the blood. Between 30 and 60 per cent of this total dose was delivered during the first twenty-four hours. The pertinent data are given in Table II.

TABLE II: DETAILS OF DOSAGE

Date of Therapy Dose	Dose Administered in mc.	Volume Dose in Megagram rep	Dose in rep	Dose in rep During First 24 Hours
9/27/48	104	5.88	73.7	45.0
11/24/48	117	5.25	78.2	40.0
1/19/49	133	10.1	125.0	41.5
2/24/49	212	19.3	241.0	87.0
3/10/49	200	17.3	217.0	82.5
6/15/49	100	9.4	118.0	31.8
11/18/49	135	17.4	218.0	59.0
7/27/50	104	16.6	208.0	114.0

SUMMARY

1. A patient with papillary follicular adenocarcinoma of the thyroid gland with multiple bony and soft-tissue metastases was treated with 1,246 millicuries of radioactive iodine (I^{131}) over a period of more than two years.

2. This patient, hopelessly involved with advanced metastatic carcinoma on admission, has been clinically well for two years. His improvement began only two months after institution of radioiodine therapy.

3. A pathological fracture of the spine of the left scapula healed under radioiodine therapy and has remained healed to date.

4. The growth potential of the metastatic lesions appears to have been arrested.

5. Striking histologic changes due to irradiation have been demonstrated in the metastatic foci.

6. Minimal changes have been demonstrated in the hemopoietic system, as well as a mild degree of renal tubular damage.

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SUMARIO

Carcinoma Tiroideo con Metástasis Múltiples y Fractura Patológica, Tratado con Exito con Radioyodo. Presentación de un Caso

Un enfermo con adenocarcinoma folicular papilar del tiroides y con metástasis múltiples en los huesos y tejidos blandos fué tratado con 1,246 milicuries de yodo radioactivo (I^{131}) durante un período de más de dos años.

El sujeto, desahuciado con carcinoma metastático avanzado, ha estado clínicamente bien por espacio de dos años, habiendo comenzado a mejorar sólo a los dos meses de iniciarse la radioyodoterapia. Una fractura patológica de la espina del omoplato izquierdo cicatrizó con dicho tratamiento y ha permanecido así hasta la fecha. El potencial de crecimiento de las lesiones metastáticas parece haber sido estacionado, y en los focos metastáticos se han observado notables alteraciones histológicas debidas a la irradiación.

Se han descubierto mínimas alteraciones en el sistema hematopoyético, e igualmente leves lesiones de los tubos renales.

Congenital Obstruction of the Transverse Colon[1]

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THE ROENTGEN demonstration of a localized obstructive lesion in the transverse colon due to anomalous development of the mesentery is an unusual experience and worthy of record.

Wm. E. Ladd was among the first to call attention to congenital obstruction of the intestines in the newborn. The great majority of congenital obstructive lesions reported in the literature have been in the duodenum, ileum and jejunum, with but rare instances in the large bowel. Miller (7) reported 14 cases of congenital obstruction, 6 in the jejunum and 8 in the duodenum, with none involving the colon. Ladd (5) stated that obstruction is not a rare condition in the duodenum, reporting 10 cases due to congenital bands and failure of rotation of the cecum, which is attached to the posterior abdominal wall across the duodenum. No case of large bowel obstruction is included in this series. Ladd and Gross (4) point out that urgent clinical manifestations of congenital obstruction of the intestinal tract are apparent in the early months of life, the majority developing in the newborn period. In a much smaller group, symptoms may not become apparent until late childhood or adult life, usually in the form of chronic, recurrent abdominal pain, vomiting, and nausea. Duckett (3) reported 6 cases of congenital intestinal obstruction, 5 of which were intrinsic obstructions in the duodenum and small bowel; in 1 case extrinsic obstruction occurred at the duodenojejunal junction. There was no case of large bowel obstruction in this series. Whitaker (2) called attention to the frequency with which congenital bands leading from the under surface of the liver to the colon are found in anatomical studies of cadavers without a history of symptoms of intestinal obstruction. Zaslow (1) reported 2 cases in newborn infants who died as a result of intestinal obstruction caused by congenital bands extending from the under surface of the liver to the hepatic flexure, producing pressure necrosis of the bowel and peritonitis. In a recent publication, Kneidel (8) reviewed the roentgen findings in 10 cases of congenital intestinal obstruction, 9 of which involved the intestine proximal to the ileocecal valve; one case of imperforate anus is included in this series. There were no instances of involvement of the intra-abdominal large bowel.

[1] Accepted for publication in March 1951.

EMBRYOLOGY

Congenital obstructive lesions of the bowel are of two types. The intrinsic obstructions are probably due to an arrest in development during the transition through which the bowel changes from a solid cord to a hollow tube, the arrest taking place prior to the twelfth week of fetal life. The extrinsic obstructions are due to an arrest in the normal return of the mid-gut from the umbilical cord and in its normal rotation. It is known that during the early weeks of embryonic development, from the sixth to the tenth week, the mid-gut grows faster than the celomic cavity, with consequent invagination of a portion of the gut into the base of the umbilical cord. After the tenth week, when the growth of the celomic cavity exceeds that of the mid-gut, the latter is again withdrawn entirely into the peritoneal cavity and lies entirely in the abdomen, rotating after the eleventh week in a counter-clockwise direction until the cecum passes successively into the right upper quadrant and then descends into the right lower quadrant. The cecum becomes peritonealized posteriorly, and the mesentery of the small bowel becomes attached to the posterior abdominal wall from the ligament of Treitz to the cecum.

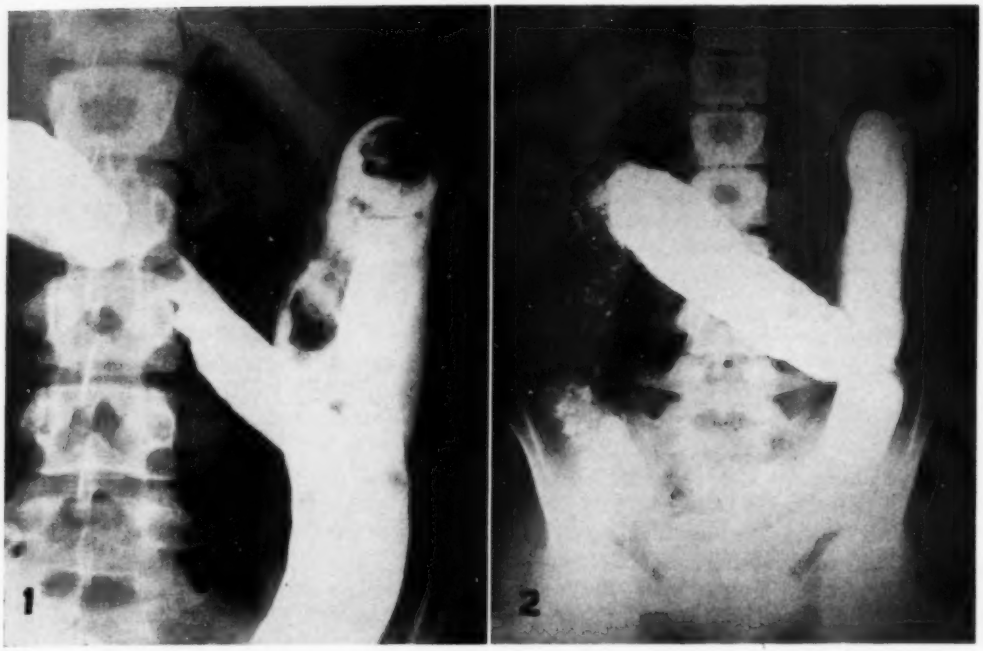

Fig. 1. Feb. 27, 1946. Constant filling defect of the transverse colon, strongly suggesting an intrinsic lesion of the bowel wall. The defect was noted in oblique positions, so that pressure from the spine was excluded.
Fig. 2. March 2, 1946. Patient asymptomatic. No defect in colonic filling is demonstrable.

CASE HISTORY

E. H., a girl aged twelve, suffered a short attack of abdominal pain, nausea, and emesis one year prior to the present illness. There was no history of previous abdominal complaints and the patient was comfortable during the interim. On Feb. 12, 1946, there was a rather acute onset of mid-abdominal pain associated at first with constipation and then with obstipation for a period of five days. Physical examination at that time revealed tenderness in the left lower quadrant. No masses were palpable. The temperature was normal. The symptoms subsided in a few days. The last attack of obstipation occurred two days before our examination, accompanied by recurrent tenderness in the left abdomen.

Roentgen Examination: Preliminary to the barium enema examination of Feb. 27, 1946, castor oil and a cleansing enema failed to empty the colon. For this reason, before administering the contrast enema, prostigmin and a second cleansing enema were given, with good results. The barium solution was noted to pass freely through the rectum, sigmoid, and ascending colon, outlining normal appearing bowel. In the transverse colon, proximal to the splenic flexure, there was demonstrated a constant narrowing of the bowel with a filling defect associated with point tenderness on direct palpation (Fig. 1). There was a slight delay in the area of stenosis, but with gentle pressure the entire right side of the colon and terminal ileum were filled. The appearance was that of an intrinsic lesion of the bowel wall. Repetition of the barium enema examination on March 2, 1946, failed to demonstrate the lesion described above. A double-contrast enema at this time showed no evidence of polypoid growth. In view of the absence of the filling defect and narrowing of the transverse colon at a second examination, it was felt that we were not dealing with an intrinsic lesion of the transverse colon but most likely with some type of extrinsic pressure effect from a congenital band producing intermittent partial obstruction.

Laparotomy was performed on March 6, 1946, by Dr. Elmer Milch. The stomach was reflected upward, exposing the transverse colon. Nothing could be palpated in the lumen of the bowel, but there was a congenital fold of peritoneum, running from the aorta posteriorly to the transverse colon, in which was situated the left colic artery and its branches. Pressure from this band was responsible for the localized narowing of the transverse colon. Because most of the blood supply to the descending colon and splenic flexure was contained in this peritoneal fold, it was decided that it could not be cut at its origin. Consequently, it was cut near its junc-

tion with the transverse colon, and the anterior and posterior layers of bowel peritoneum were gently separated, freeing the colon. It was then found that this congenital fold was connected with the ligament of Treitz, and upon its severance the duodenojejunal junction came into view, for the first time approximating a normal appearance.

Postoperative Diagnosis: Recurrent obstruction of the transverse colon due to congenital malformation in the development of the peritoneum involving the left colic artery.

The postoperative course was uneventful. During the four-year period of observation following the operation the patient has been entirely asymptomatic, with return of normal bowel habits.

COMMENT

Extrinsic pressure effects causing stenosis of the large bowel due to congenital adhesive bands are extremely rare, particularly in the absence of failure of rotation of the intestine. The lesion that we observed had to be differentiated from an intrinsic stenosis. In this case, the failure to re-demonstrate, in a second barium enema examination, the filling defect observed in the transverse colon only a few days earlier precluded the presence of an intrinsic deformity, and it was felt that the roentgen changes were most likely due to extrinsic pressure from some type of congenital band.

SUMMARY

A case of recurrent obstruction of the transverse colon due to congenital malformation in the development of the peritoneum, involving the left colic artery, is reported.

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SUMARIO

Oclusión Congénita del Colon Transverso

El caso comunicado es de obstrucción recurrente del colon transverso en un niño de doce anos, debida a un pliegue congénito de peritoneo que iba por detrás de la aorta hasta el colon transverso y contenía la arteria cólica izquierda y las ramas de la misma. El diagnóstico de oclusión extrínseca fué indicado por no haberse podido descubrier en el segundo examen con enema de bario un nicho observado anteriormente. En la operación se descubrió que el pliegue estaba unido al ligamento de Treitz. Una vez resecado, los síntomas desaparecieron.

Use of the Nine and One-Half-Inch Roll-Film Cassette with Conventional Spot-Filming Fluoroscopic Tables for Angiocardiography[1]

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CHIEFLY TO SATISFY the needs of angiocardiography and cerebral angiography, many ingenious devices have been developed for producing a rapid series of radiographs. The basic requirement is to be able to change film rapidly between automatically co-ordinated exposures. Because of practical considerations of bulk and size, most devices using cut-film cassettes limit the radiographs available in any one series to a number inadequate for complete angiocardiographic studies. Furthermore, the weight and inertia of conventional cassettes make sufficiently rapid changing of film impracticable. Hand-operated devices within these limitations have been used for many years, most of them homemade. The cassette principle was developed to a high degree by Scott and Moore in their tautograph (1). In Sweden it was carried further by the use of special light-weight reinforced cardboard cassettes; with the apparatus devised by Fredzell, Lind, Ohlson, and Wegelius (2) up to 25 such cassettes can be exposed in each of two right-angle planes simultaneously every two seconds.

The development of the automatic roll-film photofluorographic camera and roentgen cinematography offered new means for rapid serialography, with the advantages of mechanical simplicity and the convenience of small bulk. Certain disadvantages, however, as compared to direct radiography, prevented general acceptance of the procedure for angiocardiography. The chief of these was the excessive radiographic exposure necessary, resulting in severe limitations due to conventional x-ray tube tolerance. Another was the small image size and some loss of photographic definition, especially in the examination of infants and young children. The adaptation of the Schmidt-Helm reflecting camera principle to photofluorography greatly reduced the amount of exposure necessary (3) but slowed the maximum speed of serialography with film larger than 35 mm. because of the necessity of mechanically "shaping" each film frame into the curved surface necessary for adequate focus before each exposure. For these and other reasons, direct radiography is still considered the method of choice.

The roll-film cassette principle embodies much of the mechanical simplicity and ease of film handling of the photofluorographic camera, but still retains the advantages of direct radiography. During each exposure the film is held between two intensifying screens mounted on a mechanism for separating them from the film during film travel between exposures, the whole being electrically phased with the x-ray circuit.

Dr. F. J. Hodges of Ann Arbor has recently developed a model using 12-inch roll film, which provides for as many as six exposures per second (4). In Europe there is now available an instrument devised by Dr. A. Gidlund which takes two simultaneous 12 × 12-inch exposures at right angles to each other on roll film at a rate of 8 pairs per second, with provision for fluoroscopic control of positioning. This latter apparatus requires a rather specialized separate radiographic installation.

The most popular roll-film cassette in this country is an adaptation of the Fairchild aerial camera magazine, which explains the selection of 9 1/2-inch roll film (5). Two exposures per second are possible, thought by some investigators to be less than the desirable number for some phases

[1] Accepted for publication in April 1951.

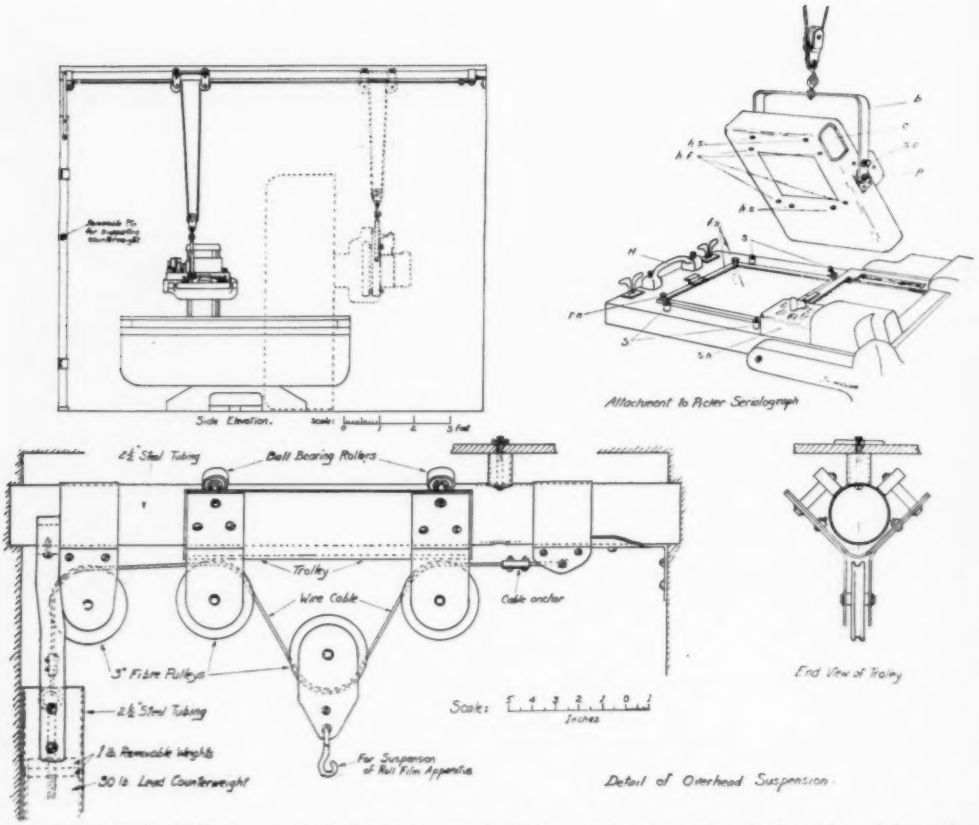

Fig. 1. Drawing indicating method of attachment of roll-film cassette to serialographic table and details for an overhead counterweight system. The cassette is suspended by a rigid bale, *b*, and pivoted, *p*, at center of gravity. It is stabilized in vertical and horizontal "ready" positions by a spring catch, *s.c.* The cut out segment, *c*, is to accommodate the serialographic selector housing, *s.h.* Four holes, *h.s.*, are for attachment to studs, *s*; 4 holes, *h.f.*, accommodate the bolts on which the thumb-nuts, *t.n.*, hold the fluoroscopic screen assembly, *f.s.*, which is removed before attaching the cassette.

of angiocardiographic study. Clinically the cassette is used by adaptation to conventional pedestals and simple radiographic tables (6).

Beside the debatable drawback of limitation to two exposures per second, there are other practical disadvantages to the pedestal and table use of the 9 1/2-inch roll-film cassette. The size of the aperture—9 inches square—requires very accurate positioning to include the average adult heart and great vessels, an important consideration in angiocardiography, where repetition of the procedure is undesirable. Test exposures on the roll-film device are wasteful and entail much time and effort, so that fluoroscopic control of positioning would be highly desirable. For the average busy general hospital department, use of special equipment and space for occasional specialized serialographic procedures is difficult to justify economically. It would be desirable to have some simple method of attaching the roll-film cassette to existing conventional equipment only when needed. With the usual arrangements for angiocardiography, there are created serious radiation hazards to operating personnel—even exposure to the primary beam in most instances—unless cumbersome protective equipment is used. Accurate primary beam limitation and built-in protection from secondary radiation would in large part eliminate such hazard.

It seemed to us that some means of optional attachment of the roll-film device to the serialographic assembly of a high-capacity modern conventional fluoroscopic tilt table would offer a solution of these problems, providing, in addition, maximum versatility and flexibility. The chief stumbling block was the weight of the roll-film device, approximately 60 lb. This was handled by the construction of a simple, unobtrusive overhead counterbalance system, designed to eliminate stress from the serialographic tower assembly due to the attachment of the roll-film device in any table position. Figures 1 and 4 are reproductions of a schematic drawing and photograph, respectively, of this arrangement, in horizontal position.

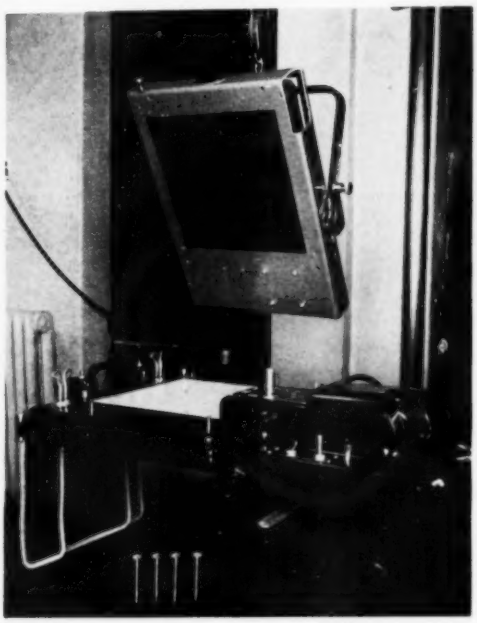

Fig. 2. Cassette tilted from usual horizontal ready position to better show the base, before removal of screen and attachment to serialograph.

The serialographic table in our department required only a few minor alterations for attachment of the frame of the roll-film device. Figures 2 and 3 and the semischematic drawing in Figure 1 illustrate the adaptations of cassette frame and the serialograph for attachment. The code letters below refer to those on the drawing. The handle, *H*, was moved out about half an inch to permit centering of the device. This will be unnecessary with the new design for the roll-film device, which will have considerably less overall width. A segment of the corner, *c*, was cut out to accommodate the serialographic selector housing, *s.h.*, which will also be unnecessary with the new design. Four threaded studs, *s*, were mounted permanently on the serialograph for attaching the device. The screws holding the fluoroscopic screen frame, *f.s.*, were replaced by permanently mounted bolts, and the frame held by thumb-nuts, *t.n.*, to facilitate the removal of the screen before attaching the roll-film device. For further convenience, the screen and lead glass may be mounted as a unit in a new frame provided with simple handles.

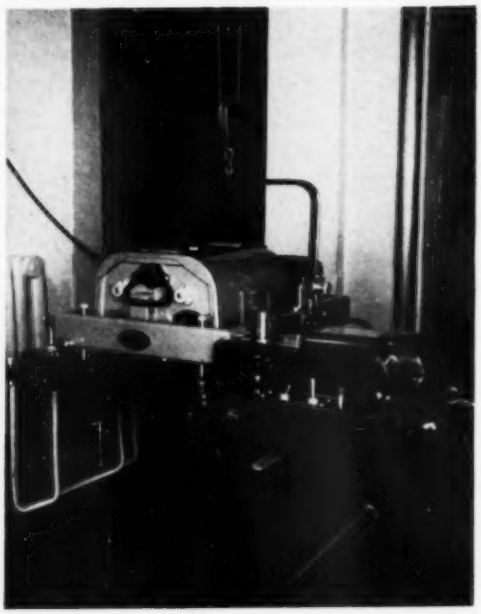

Fig. 3. Cassette attached and ready for operation.

The roll-film cassette frame was drilled with eight holes, four to receive the mounting bolts (*h.s.*), and four through which the fluoroscopic frame bolts project when the

Fig. 4. Apparatus ready in horizontal position for injection and angiocardiography

device is in place (*h.f.*). The latter were not used for mounting the device, as they were not considered strong enough and were too near the edge of the fluoroscopic screen aperture on the serialograph. Long thumb-nuts, seen on the table in Figure 2 and in place in Figure 3, are attached when the device is in place. For suspension from the counterbalance the frame is supported by a rigid steel bale, *b*, pivoted (*p*) at the center of gravity of the entire device. A two-position spring catch, *s.c.*, provides stability in horizontal and vertical "ready" positions. This was mounted on the tower side to prevent interference with the shutter controls. It will be noted that the grid slide has been removed from the roll-film device, since no added grid is necessary. The built-in serialographic grid serves instead.

The lower half of Figure 1 shows the construction details of the counterbalance assembly, which permits free, effortless movement of the roll-film device, either free or attached, vertically and horizontally along the table axis. Thus relieved of any unusual strain, the conventional tower locking devices are adequate for immobilization of the device in radiographic position. With changes in the number of removable counterweights for different amounts of film, counterbalance can be easily adjusted to permit suspension of the roll-film device in any convenient ready position during fluoroscopic positioning, etc., before actual attachment. Cable length is adjusted for maximum elevation

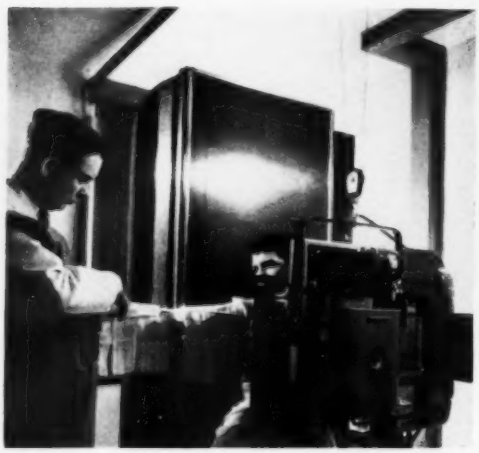

Fig. 5. Apparatus ready for vertical angiocardiography.

of the counterweight with the roll-film frame resting on the horizontal table. A removable pin can be inserted under the weight in this position to keep the suspension hook within reach and allow easier attachment of the device to that hook. With the device resting on the end of the table, slight elevation of that end will provide slack enough for easy attachment without lifting. Lowering the end takes up the slack, suspends the device, and permits removal of the counterweight pin in readiness for operation. Reversing the procedure permits easy detachment, after which the suspension hook and pulley may be fastened out of the way beside the counterweight housing. Alternate suggestions for ceiling or wall suspension of the horizontal steel tube are made. In the case of ceiling suspension where adequate support is provided, the toggle bolts are made

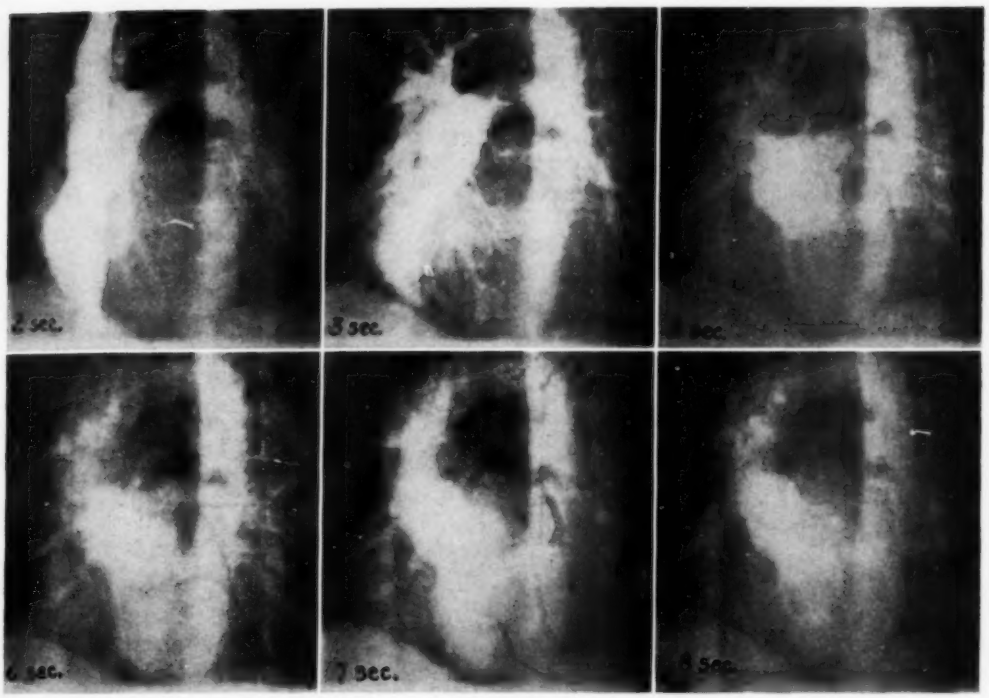

Fig. 6. Frames taken at two, three, five, six, seven, and eight seconds from angiocardiogram on large adult male with chronic syphilitic aortitis and aortic insufficiency, for aortic mensuration. Right heart and pulmonary artery filling is seen at two and three seconds; the pulmonary arterial system is filled at five seconds, and the pulmonary veins, left heart, and aorta at six, seven, and eight seconds.

accessible through slightly larger holes in the under side of the tube opposite each bolt.

The materials for the counterweight system are few and easily acquired. The pulleys, ball-bearing rollers, and counterweight cable were obtained from an x-ray company service department, and the other materials either from a hardware supply house or about the hospital machine shop. All work except the electrical connections was done by a hospital machinist. The total cost of parts and materials was less than $100.00. With the mechanical advantage of two inherent in the suspension, the lead counterweight need weigh only about 30 lb.

With use in the upright position, as shown in Figure 5, the table footboard serves as a seat. With the serialograph locked against the patient's chest and a compression band loosely applied across the chest, there is no opportunity for fall and injury during the brief syncope which sometimes occurs following rapid intravenous injection of a contrast medium. It will be noted from Figures 4 and 5 that in both positions provision is made for the desired postero-anterior radiographic projection, as well as maximum convenience for intravenous injection.

The radiographic disadvantage of the somewhat reduced anode-film distance and slightly increased part-film distance as compared with standard procedures, has not proved serious. The quality of the angiocardiograms has not been noticeably affected, and necessary exposures have been reduced slightly. Figure 6 is a typical example of selected frames from a heart mensuration study on a large adult male with chronic syphilitic aortitis.

Radiographic tube tolerances permit unlimited exposures even through the adult

abdomen at 200 ma. up to 100 kv.p. The average adult oblique chest requires only one-twentieth of a second or less. All technics use the built-in grid, and are similar enough to those with the conventional cassette spot-filming device to permit testing where technical factors are in doubt before exposure of the roll-film.

For cerebral angiography the patient may be placed directly on the table for both lateral and anteroposterior views, or a stretcher with a radioparent extension for the head may be used perpendicular to the serialographic table. The latter can then be raised to permit lateral radiography without the necessity of turning the head. The roll-film cassette on the serialographic table is also well suited to paravertebral aortic injection technics for aortography, renal arteriography, nephrography, and placentography, especially since, again, the desired anteroposterior radiographic position is prone, permitting maximum convenience for aortic injection.

In conclusion, the following advantages may be listed for the adaptation of the roll-film device to the serialographic table:

1. It eliminates the necessity of accessory apparatus and additional space in the department; even the grid is not needed.

2. It permits fluoroscopic control of radiographic positioning in angiocardiography, with ready check on radiographic technic.

3. It utilizes the well designed radiation protection of the modern serialographic table and reduces patient exposure by limiting the primary beam to the necessary field.

4. It provides convenience and versatility of positioning, including better positioning for injection technics.

5. Adaptation to most modern serialographic tables is simple and inexpensive, with the use of materials and facilities available to most general hospital engineering departments.

SUMMARY

A method of adapting the 9 1/2-inch roll-film device to a modern spot-filming fluoroscopic table is described, including construction details and method of operation. The advantages of such a system are presented.

NOTE: The author gratefully acknowledges the invaluable assistance of Mr. Eric Roicke of the Brooklyn Hospital Engineering Department in construction and suggestions for mechanical design; the suggestions of Mr. Ivan Gambrell of the Picker X-Ray Corporation for mechanical design; the photography provided by Mr. George Barham and the photographic staff of the Fairchild Camera & Instrument Corporation, and copying by Mr. Earl Thomson of the Brooklyn Hospital.

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SUMARIO

Empleo Angiocardiográfico de los Chasis para Rollos de Películas de 23.75 Cm. con las Mesas Corrientes para Fluoroscopia Instantánea

El método descrito permite adaptar a una mesa moderna para roentgenoscopia instantánea el dispositivo utilizado para rollos de película de 23.75 cm. en la serialografía rápida. Esto exige la construcción de un sencillo sistema aéreo de equilibrio que elimine, en cualquier posición de la mesa, la tensión que podría producir en

la instalación de la torre serialográfica el enlace con el chasis destinado a películas en rollo.

Cabe citar las siguientes ventajas derivadas de dicha adaptación del dispositivo para rollos de películas a la mesa serialográfica:

Elimina la necesidad de aparatos accesorios y más espacio en el departamento: no se necesita ni la rejilla.

Permite la fiscalización roentgenoscópica de las posiciones radiográficas en la angiocardiografía, con fácil comprobación de la técnica radiográfica.

Utiliza el bien concebido resguardo contra la irradiación de la moderna mesa serialográfica y reduce la exposición del enfermo por limitar el haz primario al campo necesario.

Aporta mayor conveniencia y versatilidad en las posiciones, incluso mejor posición para las técnicas de inyección.

La adaptación a las más modernas mesas de serialografía es sencilla y poco costosa, pues utiliza materiales y medios a la disposición de la mayor parte de los departamentos de ingeniería de los hospitales generales.

A Preliminary Report on Radiography in Rapid Sequence[1]

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THE RECENT GREAT increase in the use of contrast substances for study of the various vascular systems has emphasized the inadequacy of existing commercial and individually produced machines for rapid transport of film. During the past four years the design of such an apparatus has been under investigation at the Massachusetts General Hospital, and the preliminary model to be described here has been completed.

Certain fundamental premises were held from the early days of this study, constituting the requirements of the machine.

(1) Since present-day contrast substances are dangerous and may result in fatalities, particularly where multiple injections are necessary, the machine must be as simple as possible to avoid technical failures. This is a strong argument against any complicated mechanical device with elaborate systems of gears and gear trains.

(2) An attempt should be made to obtain simultaneous sets of films at right-angle projections to one another to reduce the amount of contrast substance required and at the same time increase materially the information obtained from each injection. This criterion, like the first, was predicated on reports of fatalities following multiple injections, necessitated either by failure of apparatus or by the need of additional diagnostic information.

(3) Films must be of the best possible technical quality and of adequate size. Much thought was devoted to the possibility of using roll film, either in an existing commercial device or in an individually designed modification. This principle was discarded because of the very real problem of effecting uniformly good screen contact at the speeds desired, and because it was felt that moving rolls of film of the projected size at rapid rates of speed would require elaborate and therefore vulnerable machinery. Moreover, the physical difficulty in processing large rolls of film is quite significant.

Photofluorography was discarded because of the lack of detail in such films and the excessive amounts of radiation required.

(4) A rapid sequence of films in a short space of time, especially in the case of angiocardiography, was recognized as a prerequisite. The device should be readily adjustable to varying speed combinations for different problems.

(5) The amount of radiation to be delivered to the patient in any diagnostic procedure must be kept to a minimum safe figure.

These requirements, with the exception of the second (right-angle projection), have been met in the device to be described here.

The apparatus (Fig. 1) is a separate unit of which the basic element is a stack of twenty specially constructed cassettes accommodating film measuring 10 × 12 inches. These rest on a platform which rides on roller bearings on five rods. The weight of the platform and cassettes is supported by six coil springs. Each cassette utilizes contact screens and is backed by sufficient lead to prevent appreciable fogging of the next film. Above the top cassette a stationary criss-cross grid is held in position.

The cassettes are alternately moved and held in position for exposure by the use of a strong cord which is interwoven through the entire pile (Fig. 2). This ingenious, simple, and efficacious method was sug-

[1] From the Department of Radiology, Massachusetts General Hospital, Boston, Mass. Accepted for publication in April 1951.
This work has been supported by a grant from the National Heart Institute. Contact screens were donated by Eastman Kodak Company and the Patterson Screen Division of E. I. du Pont de Nemours & Co., Inc.

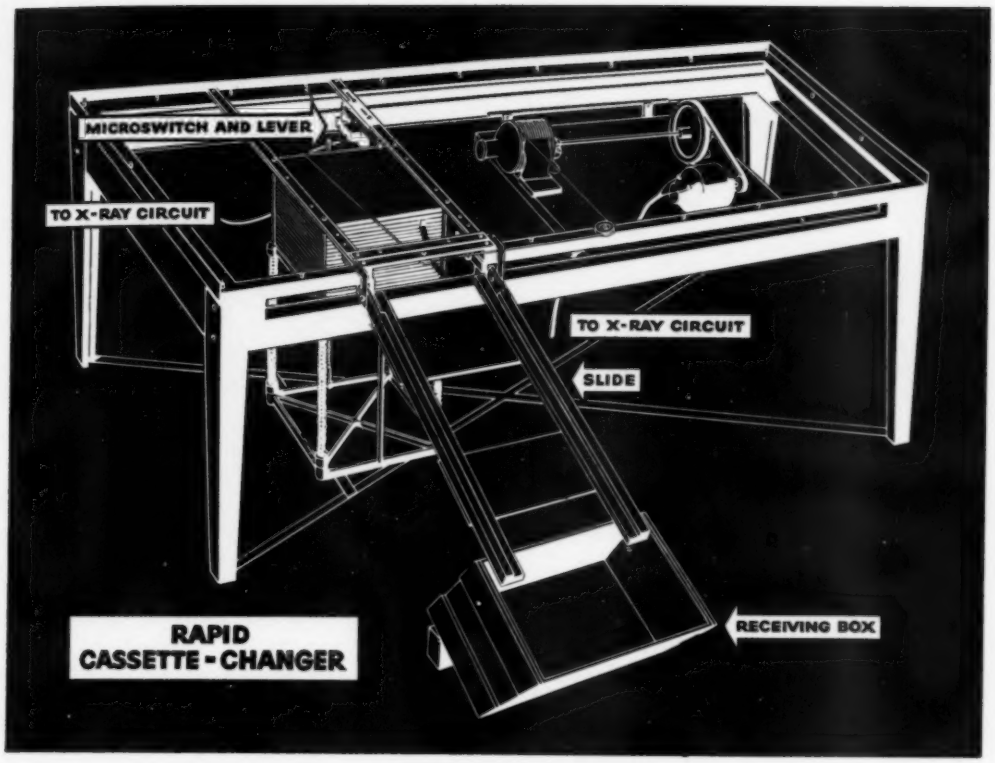

Figure 1

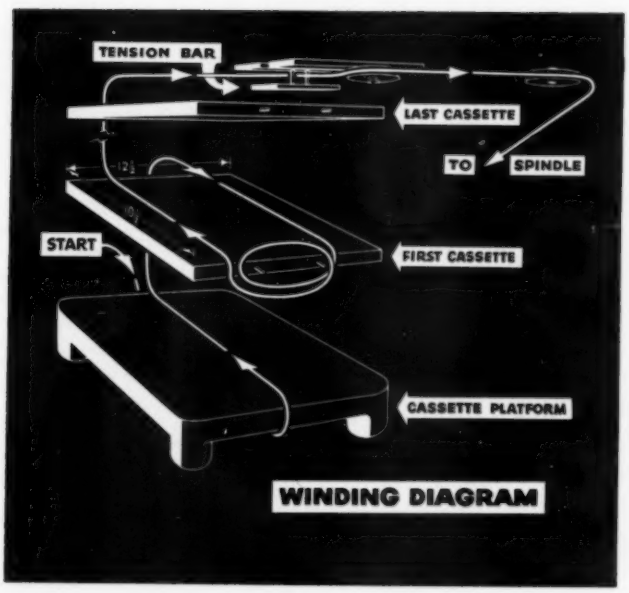

Figure 2

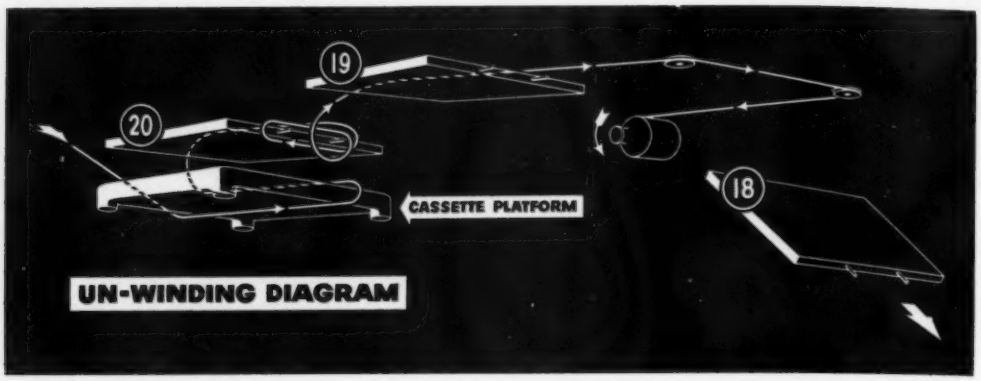

Figure 3

gested to the authors by Dr. Cesare Gianturco, who developed the first practical model.[2] This cord, a 78-pound test braided nylon fishing line, is wound on a spindle driven by a V-belt from an electric motor. By utilizing spindles of varying diameters the speed of transport of the cassettes can be changed readily and great flexibility of operation is permitted. After being exposed, each cassette is pulled off the top of the pile, slides down a chute, and is collected in a receiving box (Fig. 3).

As each cassette rises into position, it closes a micro-switch which in turn activates the timer on the control board of the x-ray machine; this timer terminates the exposure at the predetermined interval. The rapid cassette changer is wired into the circuit of the x-ray apparatus as an integral part, so that pressing the starter switch of the x-ray control panel starts the electric motor which winds up the cord, in turn moving the top cassette. Certain safeguards have been incorporated into the installation of this device to obviate, in so far as possible, failure for mechanical or electrical reasons.

[2] Am. J. Roentgenol. **62**: 741, 1949.

Cassettes can be exposed at rates up to six per second, with individual exposure times of 1/30 or 1/60 second. Voltages employed to date have been in the range of 100 to 125 kv. With these factors, film detail has been consistently good, and exposure to the patient has not exceeded 8 r for the entire twenty films. During the time that the machine has been in use, it has been found readily applicable to angiocardiography, cerebral angiography, retrograde aortography, and aortic nephrography.

The x-ray machine utilized is a standard Westinghouse 500-ma. machine with electronic timing and contacting and certain modifications in the control panel. This apparatus is capable of consistently repetitive exposures at high kilovoltage at rates up to eight exposures per second and has proved itself reliable.

NOTE: Acknowledgement is made to Mr. James Hightshoe of Westinghouse Electric Corporation, who devoted painstaking care and much time to the installation of the x-ray apparatus and its integration with the rapid cassette changer.

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SUMARIO

Comunicación Preliminar sobre la Radiografía en Rápido Turno

Los AA. describen un sencillo aparato para obtener radiografías de buena calidad en sucesión rápida (6 por segundo) sin llevar radiación excesiva al enfermo. La característica esencial es una pila de 20 chasis construídos *ad hoc* que reciben pelí-

culas de 25 × 30 cm. y reposan en una plataforma que se mueve sobre cojinetes de rodillos en cinco barras. Los chasis se mueven y mantienen en posición alternativamente con un recio cordel de nilón, entretejido a través de la pila. El cambiachasis está unido por alambre al circuito del aparato de rayos X como parte integrante del mismo, de modo que la compresión de un conmutador del tablero de control de los rayos X echa a andar el motor eléctrico que devana el cordel, moviendo el primer chasis. A medida que cada chasis sube a tomar posición, cierra un microconmutador que a su vez activa el cronógrafo del tablero de manera que puede terminarse la exposición fácilmente en un plazo predeterminado.

El aparato ha resultado ser aplicable a la angiocardiografía, la angiografía cerebral, la aortografía retrógrada y la nefrografía aórtica.

EDITORIAL

The Anatomy of Research

"Research" is a word that has shades of meaning. The medical student who consults one or two books and a few articles in preparing a paper on Sir William Osler is doing research of a kind; Harvey Cushing did research on an entirely different plane for the writing of his classic biography. The teen-age boy who thoughtfully dissects the brain of a cat is a researcher in one sense of the word but it is a sense quite different from that applying to the professional investigator in neurology. Only that form of research deserving to be recognized as such in medicine and allied sciences is characterized here. The principles of such research have been set forth many a time and by persons whose approaches are variously shaped by the fields in which they work. Yet there is general agreement on basic principles. There is no more able an exposition than the one by Claude Bernard (1); written nearly seven decades ago, the book describes essentials of scientific method that are permanent.

As a beginning, let research be defined by relating the effort of an individual to the field in which his investigation lies. Research, from this standpoint, may be viewed as an activity that promises to add something to what is already known. Its end is not merely the satisfaction of the curiosity of the researcher, and his knowledge alone is not the measure of what is already known; the amassed literature bearing on the topic of investigation is the frame of reference. Here, then, is one important difference between the student and the scholarly biographer, a difference between the boy and the professional neurologist. The additions to the store of knowledge are various: the entirely new, the old approached in new ways, the old that is either verified or opened to question. The word "promises" was inserted in the definition to emphasize that results are not always forthcoming in spite of careful planning and execution. It should be remembered, too, that promise of results in one direction may have unforeseen yields, as witnessed by the many discoveries made by "accident" in the course of investigations designed for purposes unrelated to these discoveries.

It is of interest next to examine two unlike aims of research. A distinction is made between applied science and "pure" science. An outlook for some usefulness is the criterion of research in applied science, regardless of whether the outlook is actually fulfilled in a specific investigation. Cohn's (2) succint statement illustrates this point of view: "The ultimate meaning or purpose of medical research is to rid men of diseases, to protect them from maladies with which they are threatened, to relieve them of discomforts once they are established." Dale's (3) phrasing of the same thought in regard to medical research is that "material benefit to human life and health must surely be accepted as the ultimate aim." Any research that is clearly directed toward a practical accomplishment is in applied science. Research in "pure" science is undertaken without any concern as to whether the findings may be applied toward human benefit or otherwise; it is a search for new knowledge for its own sake. Scientists engaged in such studies are sometimes chided for wasting time, since they are unable to point to practical applications of their work. They are asked "Of what use is it?" A famous reply is in the form of another question, "Of what use is a baby?" Any person who is not convinced of "the

usefulness of useless knowledge" should read Flexner's (4) spirited defense of pure science. After presenting examples, he writes: "The history of science for two thousand years proves conclusively that no one can foretell or predict or plan the outcome of the untrammeled roving of the human spirit, searching for truth and truth alone.... Let us therefore continue our quest for the useless as well as the useful, confident that in the long run both will inure to the benefit of humanity...."

Many other specific designations of kinds of research (*e.g.*, clinical, experimental) might be characterized if space were available, but it is only necessary to say that all of them share the same fundamentals; their unlikenesses lie only in technical procedures and instrumentation.

The overall method of science is simple in principle, though complex and exacting in its operation. The workings of scientific method may be resolved into three components: the investigator himself; his research; publication of results.

There is nothing strange about the personal qualifications of the ideal researcher. Naturally, he must be equipped through special training in the field or fields related to his chosen problem. His interest must be impelling; idle curiosity will not carry him through the rigors of a real research. He must be intellectually honest, alert and meticulous in attention to details, industrious and persistent. He must have good judgment, and if he is endowed with imagination it is all the better for originality in his accomplishments. Perfection should be his goal. Remember, it is the ideal researcher here described!

The research problem germinates from an idea, and however that idea may have come to the researcher it promotes a train of thinking in which the problem takes definite form. Unless the researcher is working within an area so limited that he is already familiar with its whole literature, and thus knows at once that the problem is a worthy one, his next step is to digest every discoverable publication that touches on the subject. It might be that what seemed a problem is not so after all, that the issue had been worked over many times and finally settled. In other words, it had been put to repeated test and is now firmly incorporated in the science; it is "knowledge which has acquired impersonal validity" (5). Let it be assumed that the problem proves to involve a still undecided and important question, and that a newly developed technic affords means for its possible solution. The researcher will next plan his work in detail, taking every advantage of the recorded successes and mistakes of those who have preceded him; as the work advances the original plan may require redesigning, but a plan there must be. There is no need to consider the nature of the investigation or the devices and technical procedures employed in the specific research; in all cases the underlying principles are uniform, since they are fixed standards of scientific method. Proper safeguards are set against sources of error inherent in the objects or phenomena under investigation, in the methods and instrumentation, in the researcher himself. Observations or processes are repeated until it is clear that the results are adequately established. Accurate and complete records are essential. Interpretation of the assembled records, the drawing of conclusions from them, is the final stage of the actual research.

When all this work is done, the researcher faces still another task, the writing of an account for publication. His paper or monograph, like the actual doing of research, must conform to certain canons of scientific method. The report should embody the original data in such form that the reader is able to weigh the author's conclusions against them. The methods and materials likewise should be described fully enough that the reader can not only evaluate these items but also, if he chooses, reproduce the investigation in his own laboratory or clinic. In its organization and language the report should follow the ordinary standards of English composition.

Even the title is important; explicitness is essential to searches by future workers for publications on the topic.

In surveying accounts of researches one may find in them a series of parallels to certain obstetrical situations. Publication of good research, a research adhering to generally accepted standards, might be likened to the delivery of a healthy, normal infant who will later reproduce and continue the qualities of a desirable family stock. That research has value. When standards of scientific method are ignored or violated the outcome is unfortunate. Some researches terminate as prematures, by publication before full development has been reached. Others, the miscarriages, are blighted, and an occasional research suggests comparison to a bizarre monstrosity.

HAROLD CUMMINS, PH.D.

REFERENCES

1. BERNARD, CLAUDE: An Introduction to the Study of Experimental Medicine. (Translated by H. C. Greene.) New York, The Macmillan Co., 1927.
2. COHN, ALFRED E.: The Meaning of Medical Research. Bull. New York Acad. Med. **14:** 265–291, 1938.
3. DALE, SIR HENRY: Scientific Method in Medical Research. Brit. M. J. **2:** 1185–1190, 1950.
4. FLEXNER, ABRAHAM: The Usefulness of Useless Knowledge. Squibb Inst. for Med. Res. **1:** 19–23, 1938.
5. MINOT, CHARLES S.: The Method of Science. Science **33:** 119–131, 1911.

ANNOUNCEMENTS AND BOOK REVIEWS

EXAMINATIONS

AMERICAN BOARD OF RADIOLOGY

The deadline for filing applications for the Spring (1952) examinations by the American Board of Radiology is Dec. 31, 1951.

COLORADO RADIOLOGICAL SOCIETY

The newly elected officers of the Colorado Radiological Society are: Charles F. Ingersoll, M.D., President; W. C. Huyler, M.D., Vice-President; W. P. Stampfli, M.D., 1933 Pearl St., Denver, Secretary; Vernon L. Bolton, M.D., Treasurer.

RICHMOND COUNTY (GEORGIA) RADIOLOGICAL SOCIETY

On the evening of Sept. 20, 1951, radiologists of Richmond County, Georgia, organized the Radiological Society of Richmond County, with the following officers: L. P. Holmes, M.D., President; H. R. Osheroff, M.D., Vice-President; Wm. F. Hamilton, Jr., M.D., University Hospital, Augusta, Secretary.

The first scheduled meeting of the new Society was held on Oct. 3.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY

At the recent meeting of the Rocky Mountain Radiological Society, in Denver, Edward J. Meister, M.D., of Denver, assumed the presidency. The newly elected officers are: H. Milton Berg, M.D., of Bismarck, N. D., President-Elect; James F. Kelly, M.D., Omaha, Nebr., First Vice-President; Mark S. Donovan, M.D., Denver, Colo., Second Vice-President; Maurice D. Frazer, M.D., 1037 Stuart Bldg., Lincoln, Nebr., Secretary-Treasurer; John Bouslog, M.D., Denver, Colo., Historian. The members of the Executive Committee are: Galen M. Tice, M.D., Kansas City, Kans., D. Arnold Dowell, M.D., Omaha, Nebr., and Tom B. Bond, M.D., Fort Worth, Texas.

EASTERN CONFERENCE OF RADIOLOGISTS

The Eastern Conference of Radiologists will be held March 28 and 29, 1952, at the Hotel Statler, New York City. The following tentative program has been arranged:

Criteria for the Choice of Angiography *versus* Ventriculography in the Diagnosis of Brain Tumor, ERNEST H. WOOD

Growing Skeleton in Gargoylism; Early Lesions and Their Evolution, JOHN CAFFEY

The Diagnosis and Treatment of Neuroblastoma, ROBERT S. SHERMAN, ROBERT F. PHILLIPS, AND ROBERT LEAMING

Massive Hemorrhage from the Upper Gastrointestinal Tract, JOHN A. EVANS AND FORBES DELANY

The Roentgen Aspects of the Papilla of Vater, MAXWELL H. POPPEL, HAROLD G. JACOBSON, AND ROBERT W. SMITH

Abdominal Aortography, WILLIAM SCHLEIN

Congenital Arteriovenous Communications, CHARLES T. DOTTER AND ISRAEL STEINBERG

The Roentgen Diagnosis of Broncholithiasis, COLEMAN B. RABIN AND MORTON ZISKIND

Fish-Bone Foreign Bodies of the Upper Esophagus and Pharynx: A Clinical and Experimental Study, ARNOLD L. BACHMAN

The Problem of Personnel Protection in Diagnostic Roentgenology, LILLIAN E. JACOBSON, JOEL J. SCHWARTZMAN, AND SAUL HEISER

Some Rotation Therapy Technics Applicable to Standard Deep Therapy Machines, MORTON M. KLIGERMAN AND ELAINE GILINSON

The Effect of Single Doses of X-ray on Experimentally Induced Glioma, MARTIN G. NETSKY AND J. R. FREID

X-ray Therapy of Mongolism, IRA I. KAPLAN

Segmental Resection and Radium Implantation in the Treatment of Carcinoma of the Bladder, JOHN N. ROBINSON AND MORTON M. KLIGERMAN

A Rapid Technic in Radiotherapy of Oral Carcinoma, SIDNEY RUBENFELD

Grid Therapy for Cancer of the Lung, SIDNEY M. SILVERSTONE, WILLIAM HARRIS, AND CHARLES BOTSTEIN

X-ray and Chemotherapy in the Management of Malignant Lymphomas, VINCENT C. COLLINS AND ALFRED GELLHORN

Comparison of Tissue Doses for High Energy Radiation (1–70 mev), CARL B. BRAESTRUP

Radiologists wishing to attend the Conference should write for advance registration to Dr. Maurice Lenz, 840 Park Ave., New York 21, N. Y.

SOUTHEASTERN STATES CANCER SEMINAR

The Fifth Annual Southeastern States Cancer Seminar will be held Nov. 28–30, 1951, in the San Juan Hotel, Orlando, Fla. The faculty will include Dr. Vincent P. Collins, Dr. Alfred Gellhorn, Dr. Cushman D. Haagensen, Dr. Perry B. Hudson, Dr. Herbert Maier, Dr. Joseph J. McDonald, Dr. Milton R. Porter, Dr. Arthur P. Stout, and Dr. Gray H. Twombly, from the staff of the Francis Delafield Hospital, New York City.

Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

ANGIOCARDIOGRAPHY. ANNALS OF ROENTGENOLOGY, Vol. XX. By CHARLES T. DOTTER, M.D., Assistant Professor of Radiology, Cornell University Medical College; Assistant Attending Radiologist, The New York Hospital, and ISRAEL STEINBERG, M.D., Assistant Clinical Professor of Radiology and Medicine, Cornell University Medical College; Assistant Attending Radiologist and Physician to Outpatients, the New York Hospital; Attending Physician and Chief of Chest Clinic, Sydenham Hospital; Attending Consultant, Chest Diseases, V. A. Hospital, Bronx; Consultant in Angiocardiography, U.S.N.H., St. Albans, N. Y. A volume of 304 pages, with 635 illustrations. Published by Paul B. Hoeber, Inc., Medical Book Department of Harper & Bros., New York, 1951. Price $16.00.

THE NORMAL CEREBRAL ANGIOGRAM. By ARTHUR ECKER, M.D., Ph.D. (Neurology), Surgical Neurologist, Syracuse, N. Y. A volume of 190 pages, with 140 figures. Published by Charles C Thomas, Springfield, Ill., 1951. Price $6.50.

RADIOLOGIC PHYSICS. By CHARLES WEYL AND S. REID WARREN, JR., Moore School of Electrical Engineering, University of Pennsylvania. With a Foreword by EUGENE P. PENDERGRASS, M.D., Director of the Department of Radiology, University of Pennsylvania. A volume of 492 pages, with numerous illustrations Published by Charles C Thomas, Springfield, Ill., 2d ed., 1951. Price $10.50.

RENAL PELVIS AND URETER. By PETER A. NARATH, M.D., F.I.C.S., Adjunct Professor of Urology, New York Polyclinic Medical School and Hospital. A volume of 430 pages, with 264 figures. Published by Grune & Stratton, New York, N. Y., 1951. Price $12.50.

ROENTGEN ANATOMY (ROENTGEN ANATOMÍA). By DAVID STEEL, M.D., St. John's Hospital and Evangelical Deaconess Hospital, Cleveland, Ohio. A volume of 108 full page plates. Published by Charles C Thomas, Springfield, Ill., 1951. Price $8.00.

DIE NEUZEITLICHEN BRUSTWAND- UND EXTREMITÄTEN-ABLEITUNGEN IN DER PRAXIS. By PROF. DR. HERBERT REINDELL, Oberarzt der Medizinischen Universitätsklinik Freiburg i. Br., and DR. HELMUTH KLEPZIG, Assistent der Medizinischen Universitätsklinik Freiburg i. Br., with a Foreword by PROF. DR. LUDWIG HEILMEYER, Direktor der Medizinischen Universitätsklinik Freiburg i. Br. A volume of 180 pages, with 64 illustrations. Published by Georg Thieme, Stuttgart, 1951. Distributors for U. S. A. and Canada: Grune & Stratton, Inc., 381 Fourth Ave., New York 16, N. Y.

DIE GENERALISIERTEN TUBERKULOSEN. By DR. MED. F. SCHMID, Heidelberg. From the Universitäts-Kinderklinik Heidelberg (Komm. Direktor: Prof. Dr. H. Opitz). (Erscheint im Rahmen der "Tuberkulose-Bücherei"). A monograph of 230 pages, with 60 illustrations. Published by Georg Thieme, Stuttgart, 1951. Distributors for U. S. A. and Canada: Grune & Stratton, Inc., 381 Fourth Ave., New York 16, N. Y.

Book Reviews

VISCERAL RADIOLOGY. By EMERIK MARKOVITS, M.D., Formerly, Scientific Collaborator of the Central Radiologic Institute of the General Hospital (Holzknecht-Institute), Vienna; Head of the Radiologic Department of Elizabeth Hospital of the City of Budapest; Postgraduate Lecturer at the Central Radiologic Institute of the University of Budapest; Radiologist of the Steiner Cancer Clinic, Atlanta, Ga. A volume of 612 pages, with 682 illustrations. Published by The Macmillan Co., New York, 1951. Price $24.00.

This volume considers within the space of 562 pages the respiratory, circulatory, digestive, genitourinary and nervous systems, and adds a short chapter on the abdomen and those abdominal organs not discussed in other chapters. The respiratory and gastro-intestinal systems are more extensively discussed than the others. With the aid of 130 radiographic reproductions and 552 figures, the author considers briefly, but clearly, the salient points of anatomy, physiology, pathology and roentgenology pertaining to the principal lesions of these systems.

Obviously, the space given to the various subjects is limited, and for this reason only the major points in diagnosis are emphasized. Many of the deficiencies in the text are partially made up by the inclusion of carefully prepared tables of differential diagnosis at the end of each chapter. In these tables lies the principal value of the book. Diagrammatic figures augment the brief discussions. Finally, an extensive and well chosen bibliography of the pertinent literature is included. The index is easily used. The book is well bound and the format attractive.

This work will be found most useful by the beginner in radiology who needs an easily read and easily understood introduction to roentgenology of the visceral systems. It has little to offer the well trained radiologist.

RADIOLOGICAL SOCIETIES: SECRETARIES AND MEETING DATES

Editor's Note: Secretaries of state and local radiological societies are requested to co-operate in keeping this section up-to-date by notifying the editor promptly of changes in officers and meeting dates.

RADIOLOGICAL SOCIETY OF NORTH AMERICA. *Secretary-Treasurer*, Donald S. Childs, M.D., 713 E. Genesee St., Syracuse 2, N. Y.

AMERICAN RADIUM SOCIETY. *Secretary*, John E. Wirth, M.D., 635 Herkimer St., Pasadena 1, Calif.

AMERICAN ROENTGEN RAY SOCIETY. *Secretary*, Barton R. Young, M.D., Germantown Hospital, Philadelphia 44, Penna.

AMERICAN COLLEGE OF RADIOLOGY. *Exec. Secretary*, William C. Stronach, 20 N. Wacker Dr., Chicago 6.

SECTION ON RADIOLOGY, A. M. A. *Secretary*, Paul C. Hodges, M.D., 950 East 59th St., Chicago.

Alabama

ALABAMA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, W. D. Anderson, M.D., 420 10th St., Tuscaloosa.

Arizona

ARIZONA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, R. Lee Foster, M.D., 507 Professional Bldg., Phoenix. Annual meeting with State Medical Association.

Arkansas

ARKANSAS RADIOLOGICAL SOCIETY. *Secretary*, Fred Hames, M.D., Pine Bluff. Meets every three months and at meeting of State Medical Society.

California

CALIFORNIA MEDICAL ASSOCIATION, SECTION ON RADIOLOGY. *Secretary*, Sydney F. Thomas, M.D., Palo Alto Clinic, Palo Alto.

EAST BAY ROENTGEN SOCIETY. *Secretary*, Dan Tucker, M.D., 434 30th St., Oakland 9. Meets monthly, first Thursday, at Peralta Hospital.

LOS ANGELES RADIOLOGICAL SOCIETY. *Secretary*, Harold P. Tompkins, M.D., 658 South Westlake Ave. Meets monthly, second Wednesday, County Society Bldg.

NORTHERN CALIFORNIA RADIOLOGICAL CLUB. *Secretary*, G. A. Fricker, Sacramento Co. Hospital, Sacramento 17. Meets at dinner last Monday of September, November, January, March, and May.

PACIFIC ROENTGEN SOCIETY. *Secretary*, L. Henry Garland, M.D., 450 Sutter St., San Francisco 8. Meets annually with State Medical Association.

SAN DIEGO ROENTGEN SOCIETY. *Secretary*, R. F. Niehaus, M.D., 1831 Fourth Ave., San Diego. Meets first Wednesday of each month.

SAN FRANCISCO RADIOLOGICAL SOCIETY. *Secretary*, I. J. Miller, M.D., 2680 Ocean Ave., San Francisco 27. Meets quarterly.

SOUTH BAY RADIOLOGICAL SOCIETY. *Secretary*, Ford Shepherd, M.D., 526 Soquel Ave, Santa Cruz. Meets monthly, second Wednesday.

X-RAY STUDY CLUB OF SAN FRANCISCO. *Secretary*, Merrell A. Sisson, M.D., 450 Sutter St., San Francisco 8. Meets third Thursday at 7:45 January to June at Stanford University Hospital, July to December at San Francisco Hospital.

Colorado

COLORADO RADIOLOGICAL SOCIETY. *Secretary*, Wendell P. Stampfli, M.D., 1933 Pearl St., Denver. Meets monthly, third Friday, at University of Colorado Medical Center or Denver Athletic Club.

Connecticut

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY. *Secretary*, Fred Zaff, M.D., 135 Whitney Ave., New Haven. Meets bimonthly, second Wednesday.

CONNECTICUT VALLEY RADIOLOGICAL SOCIETY. *Secretary*, Ellwood W. Godfrey, M.D., 1676 Boulevard, W. Hartford. Meets second Friday of October and April.

District of Columbia

RADIOLOGICAL SECTION, DISTRICT OF COLUMBIA MEDICAL SOCIETY. *Secretary*, U. V. Wilcox, M.D., 915 19th St., N.W., Washington 6. Meets third Thursday, January, March, May, and October, at 8:00 P.M., in Medical Society Library.

Florida

FLORIDA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Nelson T. Pearson, M.D., 1109 Huntington Bldg., Miami. Meets in April and in November.

GREATER MIAMI RADIOLOGICAL SOCIETY. *Secretary*, Theodore M. Berman, M.D., 350 Lincoln Road, Miami Beach. Meets monthly, last Wednesday, 8:00 P.M., Veterans Administration Bldg., Miami.

Georgia

ATLANTA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, J. Dudley King, M.D., 35 Linden Ave., N. E. Meets second Friday, September to May.

GEORGIA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Robert C. Pendergrass, M.D., Americus. Meets in November and with State Medical Association.

Illinois

CHICAGO ROENTGEN SOCIETY. *Secretary*, Benjamin D. Braun, M.D., 6 N. Michigan Ave., Chicago 11. Meets at the University Club, second Thursday of October, November, January, February, March, and April at 8:00 P.M.

ILLINOIS RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, William DeHollander, M.D., St. John's Hospital, Springfield. Meets quarterly as announced.

ILLINOIS STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY. *Secretary*, Willard C. Smullen, M.D., St. Mary's Hospital, Decatur.

Indiana

INDIANA ROENTGEN SOCIETY. *Secretary-Treasurer*, William M. Loehr, M.D., 712 Hume-Mansur Bldg., Indianapolis 4. Annual meeting in May.

Iowa

IOWA X-RAY CLUB. *Secretary*, Arthur W. Erskine, M.D., 326 Higley Building, Cedar Rapids. Meets during annual session of State Medical Society.

Kansas

KANSAS RADIOLOGICAL SOCIETY. *Secretary*, Charles M. White, M.D., 3244 East Douglas, Wichita 8. Meets annually with State Medical Society.

Kentucky

KENTUCKY RADIOLOGICAL SOCIETY, *Secretary*, Everett L. Pirkey, M.D., Louisville General Hospital. Meets monthly, second Friday, at Seelbach Hotel.

Louisiana

LOUISIANA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Johnson R. Anderson, M.D., No. Louisiana Sanitarium, Shreveport. Meets with State Medical Society.

ORLEANS PARISH RADIOLOGICAL SOCIETY. *Secretary*, Joseph V. Schlosser, M.D., Charity Hospital of Louisiana, New Orleans 13. Meets first Tuesday of each month.

SHREVEPORT RADIOLOGICAL CLUB. *Secretary*, Oscar O. Jones, M.D., 2622 Greenwood Road. Meets monthly September to May, third Wednesday.

Maine

MAINE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Clark F. Miller, M.D., Central Maine General Hospital, Lewiston.

Maryland

BALTIMORE CITY MEDICAL SOCIETY, RADIOLOGICAL SECTION. *Secretary-Treasurer*, Richard B. Hanchett, M.D., 705-6, Medical Arts Bldg., Baltimore 1. Meets third Tuesday, September to May.

Michigan

DETROIT X-RAY AND RADIUM SOCIETY. *Secretary*, James C. Cook, M.D., Harper Hospital, Detroit 1. Meets first Thursday, October to May, at Wayne County Medical Society club rooms.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS. *Secretary-Treasurer*, R. B. MacDuff, M.D., 220 Genesee Bank Building, Flint 3.

Minnesota

MINNESOTA RADIOLOGICAL SOCIETY. *Secretary*, Leo A. Nash, M.D., 572 Lowry Medical Arts Bldg., St. Paul 2. Meets in Spring and Fall.

Missouri

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY. *Secretary*, Wm. M. Kitchen, M.D., 1010 Rialto Building, Kansas City 6, Mo. Meets last Friday of each month.

ST. LOUIS SOCIETY OF RADIOLOGISTS. *Secretary*, Donald S. Bottom, M.D., 510 S. Kingshighway Blvd. Meets on fourth Wednesday, October to May.

Nebraska

NEBRASKA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Russell W. Blanchard, M.D., 1216 Medical Arts Bldg., Omaha. Meets fourth Thursday of each month at 6 P.M. in Omaha or Lincoln.

New England

NEW ENGLAND ROENTGEN RAY SOCIETY. *Secretary*, L. L. Robbins, M.D., Massachusetts General Hospital, Boston 14. Meets monthly on third Friday at the Harvard Club, Boston.

New Hampshire

NEW HAMPSHIRE ROENTGEN SOCIETY. *Secretary*, Albert C. Johnston, M.D., Elliot Community Hospital, Keene. Meets quarterly in Concord.

New Jersey

RADIOLOGICAL SOCIETY OF NEW JERSEY. *Secretary*, Nicholas G. Demy, M.D., 912 Prospect Ave., Plainfield. Meets at Atlantic City at time of State Medical Society and midwinter in Elizabeth.

New York

ASSOCIATED RADIOLOGISTS OF NEW YORK, INC. *Secretary*, William J. Francis, M.D., East Rockaway.

BROOKLYN ROENTGEN RAY SOCIETY. *Secretary*, J. Daversa, M.D., 603 Fourth Ave., Brooklyn. Meets fourth Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Mario C. Gian, M.D., 610 Niagara St., Buffalo 1. Meets second Monday, October to May.

CENTRAL NEW YORK ROENTGEN SOCIETY. *Secretary*, Dwight V. Needham, M.D., 608 E. Genesee St., Syracuse 10. Meets in January, May, October.

KINGS COUNTY RADIOLOGICAL SOCIETY. *Secretary*, Marcus Wiener, M.D., 1430 48th St., Brooklyn 19. Meets fourth Thursday, October to May, at 8:45 P.M., Kings County Medical Bldg.

NEW YORK ROENTGEN SOCIETY. *Secretary*, Irving Schwartz, 45 E. 66th St., New York 21.

NORTHEASTERN NEW YORK RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, John F. Roach, M.D., Albany Hospital, Albany. Meets at University Club, Albany, second Wednesday, October, November, and March. Annual Meeting in June to be announced.

ROCHESTER ROENTGEN-RAY SOCIETY. *Secretary-Treasurer*, George Gamsu, M.D., 191 S. Goodman St. Meets at Strong Memorial Hospital, last Monday of each month, September through May.

North Carolina

RADIOLOGICAL SOCIETY OF NORTH CAROLINA. *Secretary*, James E. Hemphill, M.D., Professional Bldg., Charlotte 2. Meets in May and October.

North Dakota

NORTH DAKOTA RADIOLOGICAL SOCIETY. *Secretary*, P. H. Woutat, M.D., 322 Demers Ave., Grand Forks.

Ohio

OHIO STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Edward C. Elsey, M.D., 927 Carew Tower, Cincinnati 2. Meets with State Medical Association.

CENTRAL OHIO RADIOLOGICAL SOCIETY. *Secretary*, Frank A. Riebel, M.D., 15 W. Goodale St., Columbus. Meets second Thursday, October, December, February, April, and June, 6:30 P.M., Columbus Athletic Club, Columbus.

CLEVELAND RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Mortimer Lubert, M.D., Heights Medical Center Bldg., Cleveland Heights 6. Meets at 6:45 P.M. on fourth Monday, October to April, inclusive.

GREATER CINCINNATI RADIOLOGICAL SOCIETY. *Secretary*, Lee S. Rosenberg, M.D., Jewish Hospital, Cincinnati 29. Meets first Monday, October through May.

MIAMI VALLEY RADIOLOGICAL SOCIETY. *Secretary*, Geo. A. Nicoll, M.D., Miami Valley Hospital, Dayton. Meets monthly, second Friday.

Oklahoma

OKLAHOMA STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, W. E. Brown, M.D., 21st and Xanthus, Tulsa 4. Meets in October, January, and May.

Oregon

OREGON RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, J. Richard Raines, M.D., Medical-Dental Bldg., Portland 5. Meets monthly, second Wednesday, October to June, at 8:00 P.M., University Club.

Pacific Northwest

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Sydney J. Hawley, M.D., 1320 Madison St., Seattle 4. Meets annually in May.

Pennsylvania

PENNSYLVANIA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, James M. Converse, M.D., 416 Pine St., Williamsport 8. Meets annually.

PHILADELPHIA ROENTGEN RAY SOCIETY. *Secretary*, George P. Keefer, M.D., American Oncologic Hospital, Philadelphia 4. Meets first Thursday of each month at 8:00 P.M., from October to May, in Thomson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY. *Secretary-Treasurer*, Edwin J. Euphrat, M.D., 3500 Fifth Ave., Pittsburgh 13. Meets monthly, second Wednesday, at 6:30 P.M., October to May, at Webster Hall.

Rocky Mountain States

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Maurice D. Frazer, M.D., 1037 Stuart Bldg., Lincoln, Nebr.

South Carolina

SOUTH CAROLINA X-RAY SOCIETY. *Secretary-Treasurer*, Henry E. Plenge, M.D., 855 N. Church St., Spartanburg. Meets with State Medical Association in May.

South Dakota

RADIOLOGICAL SOCIETY OF SOUTH DAKOTA. *Secretary-Treasurer*, Marianne Wallis, M.D., 1200 E. Fifth Ave., Mitchell. Meets with State Medical Society.

Tennessee

MEMPHIS ROENTGEN CLUB. *Secretary*, John E. Whiteleather, M.D., 899 Madison Ave. Meets first Monday of each month at John Gaston Hospital.

TENNESSEE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, J. Marsh Frère, M.D., 707 Walnut St., Chattanooga. Meets annually with State Medical Society in April.

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DALLAS-FORT WORTH ROENTGEN STUDY CLUB. *Secretary*, X. R. Hyde, M.D., Medical Arts Bldg., Fort Worth 2. Meets monthly, third Monday, in Dallas odd months, Fort Worth even months.

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UTAH STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Angus K. Wilson, M.D., 343 S. Main St., Salt Lake City. Meets third Wednesday, January, March, May, September, November.

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ABSTRACTS OF CURRENT LITERATURE

ROENTGEN DIAGNOSIS

The Head and Neck

The Chest

The Digestive System

The Musculoskeletal System

Obstetrics and Gynecology

The Genito-Urinary System

The Blood Vessels

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ROENTGEN DIAGNOSIS

THE HEAD AND NECK

Carotid Angiography; Its Value in Premalignant Intracranial Conditions. Arthur A. Morris and O. Hugh Fulcher. S. Clin. North America **30**: 1783–1796, December 1950.

Every intracranial lesion of expanding nature is potentially malignant. This does not relate to the cellular content but to the fact that all of these lesions will eventually cause death by occupying space and by producing pressure on the brain. Thus a small aneurysm, an arteriovenous fistula, an intracerebral hematoma, or a brain abscess may be considered "premalignant," *i.e.*, likely to end fatally.

Cerebral angiography has contributed materially to the diagnosis of intracranial aneurysms, tumors, and other space-occupying conditions. It has also afforded a method of estimating the circulation time and has aided in the preoperative pathological diagnosis of tumors.

The technic of carotid angiography is described in detail. The injection is made as rapidly as possible, only 8 c.c. of 35 per cent diodrast being used. With a seriograph 6 exposures are made in 4 seconds. Bilateral arteriography is used when necessary. In some cases pneumoencephalography and carotid arteriography have been combined.

The outstanding value of carotid angiography is in the diagnosis and management of aneurysms, arteriovenous fistulas, and hemangiomas. Only by the introduction of a contrast medium intra-arterially can the existence of these conditions be objectively demonstrated. The surgical approach can be carefully planned and adequate precautions taken. If an aneurysm has ruptured, the method will frequently determine if a localized hematoma exists.

Seven illustrations, including 4 arteriograms.

PAUL W. ROMAN, M.D.
Baltimore, Md.

Pathological Anatomy and Angiography of Intracranial Vascular Anomalies. Oscar Sugar. J. Neurosurg. **8**: 3–22, January 1951.

The author quotes Dandy as having stated that there could be but one explanation for aneurysms of the congenital type—that they have their origin in defects incident to the resolution of the early vascular bed. The basilar artery is formed from the two longitudinal neural arteries under the neural tube in the early embryo. At the line of fusion one might expect aneurysms to occur. The persistence of other primitive vessels can account for the presence of aneurysms to one side of the basilar artery, aneurysms arising from the cavernous portion of the internal carotid artery, and carotid-cavernous fistulae.

The posterior communicating artery is large in the embryo, arising directly as a division of the internal carotid artery. It usually dwindles to a small connection with the posterior cerebral artery which typically comes off the basilar artery in the adult. The communicating vessel may, however, persist as the main stem of the posterior cerebral artery, which then arises from the internal carotid artery.

Lateral and medial aneurysms of the internal carotid artery between the ophthalmic and posterior communicating vessels may be due to the persistence of remnants of the primitive ventral and dorsal ophthalmic arteries, which usually disappear.

Telangiectases are formed by the dilatation of embryonic vessels without adding muscular coats to their walls. Angiograms of such telangiectases have not yet been obtained. However, angiograms have been made of the vascular anomaly frequently classed as telangiectasis and known as Sturge-Weber disease or trigeminal encephalo-angiomatosis. These may show clusters of small vessels.

The embryonic network may at times differentiate into abnormal communications between the arterial and venous circulations. These may occur in any region of the brain, but seem to have a predilection for the rolandic area. Sometimes, what appear to be typical sac-like aneurysms develop in relation to such masses.

Hemangioblastomatous lesions of the brain are classified as tumors, but appear to be predicated on an embryologic basis, and sometimes vascular anomalies are associated with them.

Thirty-two illustrations, including 29 roentgenograms.

HOWARD L. STEINBACH, M.D.
University of California

Specific Treatment of Intracranial Aneurysms. Experiences with 143 Surgically Treated Patients. James L. Poppen. J. Neurosurg. **8**: 75–102, January 1951.

Either of two courses may be followed in the treatment of intracranial aneurysms, conservative or surgical. Conservative treatment is justifiable only in a few instances, as in bilateral multiple intracranial aneurysms, arteriosclerotic saccular aneurysms with minimal symptoms, arteriosclerotic aneurysmal dilatations that have produced no serious local symptoms, and cases in which adequate collateral circulation prevents either direct or indirect surgical attack.

The diagnosis and treatment of intracranial aneurysms cannot be determined without adequate arteriography. There should be no hesitancy in carrying out this procedure at any stage of subarachnoid bleeding. Arteriography should not be performed under local anesthesia, however, unless the superior cervical sympathetic ganglion and carotid sinus have been thoroughly anesthetized with procaine.

The indirect surgical attack consists of ligation of a large artery or arteries in the neck, usually the internal carotid artery, in an attempt to lower the intra-aneurysmal arterial pressure. This is the procedure of choice in the majority of patients in whom the aneurysm is confined to the bifurcations of the larger arteries in the circle of Willis.

Direct intracranial surgical attack should be reserved for aneurysms that do not arise from the bifurcations of the larger arteries that make up the circle of Willis unless there is an adequate neck which allows occlusion at that point without interference with the main arterial trunks. The direct intracranial attack may be combined with the indirect attack, so-called trapping, in aneurysms that are proximal to the bifurcation of the internal carotid artery or in aneurysms that have ruptured into the cavernous sinus.

Thirty-one figures, including 18 roentgenograms.

HOWARD L. STEINBACH, M.D.
University of California

Surgical Experiences with Arteriovenous Anomalies of the Brain. Robert C. Bassett. J. Neurosurg. **8:** 59–74, January 1951.

The clinician frequently sees arteriovenous anomalies of the brain in the late second or third decade of life, although the patient sometimes becomes symptomatic before that time. The most common symptom is the occurrence of focal fits which gradually increase in frequency and severity, and eventually become generalized. Headaches and repetitive episodes of subarachnoid hemorrhage are the next most common symptoms and signs. Hemorrhage may also be intracerebral.

Cerebral angiography has aided in the surgical treatment of these cases by providing precise localization of the lesions and demonstrating the major afferent arterial components. Routine roentgenograms may show an anomalous blood supply to the skull associated with the underlying anomaly of the brain. Pneumoencephalograms demonstrate focal atrophy associated with a "typical bizarre type of deformity."

If there are no objective findings of progressive neurologic deficit, uncontrolled epilepsy, intolerable pain, and recurrent bleeding, the treatment is expectant. With the progressive development of these signs and symptoms surgery is mandatory. The authors do not believe that irradiation has a place in the treatment of these lesions.

Reports of 18 cases of arteriovenous anomaly are presented. All of the patients operated upon showed an associated postoperative neurological deficit peculiar to the locus of the lesion. However, these signs usually cleared within ten days to six weeks following operation. None of the survivors was made worse by the operation. Those who had headaches are now free of them; those who had uncontrolled fits now have none, or a negligible number. There were two deaths in this series.

Twenty-five roentgenograms.

HOWARD L. STEINBACH, M.D.
University of California

Brain Revascularization After Carotid-Jugular Anastomosis Assessed by Angiography. I. M. Tarlov, B. Shure, B. S. Epstein, E. Hirsch, and R. Nissen. Arch. Neurol. & Psychiat. **64:** 847–860, December 1950.

Beck, McKhann, and Belnap made a noteworthy attempt to increase the vascularization of the brain in patients with mental retardation, convulsive disorders, and various types of sensory and motor defects (J. Pediat. **35:** 317, 1949). These investigators established an arteriovenous fistula between the common carotid artery and the internal jugular vein, thereby converting the vein into an arterial channel. They chose the right side for the anastomosis, because a colored mixture injected into the right internal jugular vein in cadavers "filled the superior sagittal sinus and all of its visible branches." They operated on 11 patients and reported their results in 4, stating that although the postoperative follow-up was limited to one, three, and five months, benefit had been obvious.

The purpose of the present study was to assess the value of the operation by means of cerebral angiography, which, it was hoped, would provide information concerning the redistribution of the blood flow after establishment of the fistula. In 3 mentally and physically retarded children an arteriovenous fistula was created in accordance with the technic described by Beck and his co-workers, and cerebral angiography with a 35 per cent solution of diodrast was performed before and at least once after the operation. The 3 case histories are given in detail.

The chief effect of the operation was to divert the stream of arterial blood from the right common carotid artery to the internal jugular vein and thence to the right transverse sinus. The number of blood vessels demonstrable in the cerebral angiogram was not increased.

Proptosis has been observed as a complication of the procedure, being attributable to progressive dilatation of retrobulbar veins. Other veins carrying arterial blood also undergo progressive enlargement. The question arises, therefore, whether other cardiovascular complications might not occur in the course of time.

This study provides no basis for optimism regarding the outcome of carotid-jugular anastomosis for increasing the vascularization of the brain.

Twenty-two roentgenograms; 3 photographs.

H. A. O'NEILL, M.D.
Cleveland, Ohio

Complications of Angiography. Rembrandt Dunsmore, William Beecher Scoville, and Benjamin Bradford Whitcomb. J. Neurosurg. **8:** 110–118, January 1951.

The authors have seen a wide variety of adverse reactions to diodrast angiography and emphasize its potential hazards. Among 108 cases in which 147 carotid angiograms were obtained with 35 per cent diodrast, there were 14 complications, of which 8 were major, including 3 deaths and 4 permanent paralyses, and 6 were minor, including 2 cases of convulsions. There did not appear to be any relationship between the complications and (*a*) open *vs.* closed technic, (*b*) the surgeon performing the procedure, (*c*) premedication, (*d*) rapidity of injection or quantity of the medium used, or (*e*) presence of hypertension. There did appear to be a direct relationship to the selection of cases, complications arising in older patients having a tendency toward thrombosis and in patients with impaired cerebral circulation from one cause or another (tumor and aneurysm).

Vasospasm probably plays the major part in causation of complications. The delayed occurrence of many of the complications suggests thrombosis following initial spasm or tissue anoxia.

The following prophylactic measures are recommended for use in those cases in which there are signs of defective cerebral circulation as indicated by age, history, or neurologic deficits:

1. Preoperative and postoperative papaverine for one and two days respectively.
2. Preoperative intravenous sodium luminal, gr. iv.
3. A general anesthetic and/or a short delay between injections.
4. In those cases in which a thrombosis develops, repeated stellate novocain blocks on alternating sides at intervals of four to six hours.

Four illustrations. HOWARD L. STEINBACH, M.D.
University of California

Dural Sinus Venography as an Aid to Diagnosis in Intracranial Disease. Bronson S. Ray, Howard S. Dunbar, and Charles T. Dotter. J. Neurosurg. **8:** 23–37, January 1951.

Two methods of visualization of the intracranial venous system have been developed by the authors:

(*a*) injection of 35 per cent diodrast through a catheter introduced into the anterior third of the superior sagittal sinus; (*b*) retrograde injection of 70 per cent diodrast into the superior bulb of the internal jugular vein through a catheter passed upward from the cubital vein.

In the normal subject, after the contrast medium is injected into the superior longitudinal sinus, it passes rapidly back through the longitudinal sinus, thence into the transverse sinuses and internal jugular veins. The other dural sinuses and the cerebral veins are not visualized, although sometimes venous lacunae along the margin of the sinus and short segments of a few superior cerebral and diploic veins are seen. Occasionally the most anterior end of the sagittal sinus and short segments of the orbital and facial veins are visualized.

Retrograde jugular venograms showed good filling of the superior and inferior petrosal sinuses and less often of the cavernous sinus and transverse sinus of the same side. There was also good filling of the vertebral, orbital, and facial veins, and the pterygoid plexus.

The most important practical uses to which these methods of demonstrating the dural venous sinuses can be put at present appear to be the demonstration of partial or complete obstruction of the superior sagittal or transverse sinuses. In the case of neoplasms obstructing a sinus this knowledge beforehand simplifies decision as to the extent to which operation for removal of the tumor should and can safely be carried. In the case of thrombosis, a means is provided for more accurate diagnosis and for evaluation of the adequacy of the anastomotic veins.

Case reports are presented illustrating abnormal patterns of the intracranial venous system (*a*) due to neoplasm invading the sagittal sinus and transverse sinus, (*b*) due to thrombosis of the sagittal sinus and transverse sinus, and (*c*) following ligation or resection of one transverse sinus.

[See also the authors' paper on this subject in Radiology **57**: 477, October 1951.]

Fifteen roentgenograms.

HOWARD L. STEINBACH, M.D.
University of California

Aseptic Lateral Sinus Thrombosis. Goodlatte B. Gilmore and Alan Austin Scheer. Arch. Otolaryng. **52**: 639–641, October 1950.

The authors report the case of a 7-year-old boy who sustained a depressed fracture of the left occipital bone extending into the left lateral sinus. A brief posttraumatic period of confusion and stupor rapidly cleared, but three weeks later progressive bilateral papilledema and retinal hemorrhages appeared, associated with a considerable and progressive elevation of spinal fluid pressure. Left jugular compression several days later did not produce the expected elevation of the spinal fluid pressure as shown on the manometer, since the left lateral sinus was occluded by a thrombus. Jugular pressure on the right produced the expected response.

In the following three weeks the retinal hemorrhages resolved, the papilledema improved, the elevated spinal fluid pressure showed a considerable decrease, and the patient continued mentally alert, but left jugular compression was still without effect. A few days later, canalization of the thrombus was manifested by a normal elevation of spinal fluid pressure following left jugular compression.

Two roentgenograms.

CORNELIUS COLANGELO, M.D.
Chicago, Ill.

Localization of Intracranial Neoplasms with Radioactive Diiodofluorescein. Robert Woolsey and George Thoma. J. Missouri M. A. **47**: 885–889, December 1950.

This article is based on 42 cases in which radioactive diiodofluorescein was used. Of these, 24 had normal records and no evidence of tumor was elicited by other methods of examination such as electroencephalogram, pneumoencephalogram, ventriculogram, or craniotomy. There was a total of 17 positive records. In 9 of these the tumor was correctly localized as proved by craniotomy or autopsy. Six suspected tumors were localized but have not as yet been proved. In 2 cases there were consistently localized areas of increased radioactivity but no lesions were found at operation. In 1 case the tumor was not localized by this method but was found at operation.

Since this is a preliminary report, no effort is made to compute the percentages of success or failure. The series is too small and the number of unconfirmed cases to date too large to allow arrival at any significant statistical results. In the 13 cases with operative or necropsy substantiation, 9 tumors, as mentioned above, were correctly localized and a subdural hematoma was not localized. One tumor was missed and 2 were localized incorrectly. Results, therefore, were correct in 10 of 13 cases.

The technic of the procedure is carefully reviewed and sketches of the areas where the readings are taken are nicely delineated. The cases with positive findings are presented in some detail.

Five illustrations.

S. F. THOMAS, M.D.
Palo Alto, Calif.

Radioactive Diiodofluorescein in Diagnosis and Localization of Central Nervous System Tumors. Loyal Davis, John Martin, Moses Ashkenazy, George V. LeRoy, and Theodore Fields. J. A. M. A. **144**: 1424–1432, Dec. 23, 1950.

This paper is a detailed report on the use of radioactive diiodofluorescein. The authors' own summary is complete and adequate and is given in full here. For those desiring the more technical details, the diagrams and sketches which appear in the article would be useful for setting up of such a program.

"In 200 patients suspected of having central nervous system tumors, studied by means of radioactive diiodofluorescein, the results reveal a 95.5 per cent accuracy in diagnosis in lesions verified by surgical intervention or corroborated by pneumography or angiography. The technic is simple, and instrumentation consists of a Geiger-Müller tube, a counting rate meter, and mechanical graphic recorder. There was a 91 per cent accuracy in the 95 histologically verified space-occupying lesions of the central nervous system, which included 40 gliomas, 13 meningiomas, 13 metastatic carcinomas and sarcomas, 7 pituitary tumors, 6 spinal cord tumors, 2 cerebellar hemangioblastomas, 1 acoustic neurinoma, 1 melanoblastoma, 3 unclassified tumors, 4 subdural hematomas, 1 porencephalic cyst, 2 cerebral abscesses, 1 arteriovenous fistula, and 1 granulomatous cyst. A positive radiodye test was re-

corded in 5 of the 6 verified tumors of the spinal cord.

"The affinity of radioactive dye for tumor tissue was related to the cellularity and vascular pattern of the tumor. The more malignant the neoplasm, the greater was the radiofluorescein concentration. Metastatic carcinomas and sarcomas gave counts of the highest differential range. Next were the glioblastomas and the vascular cellular meningiomas. The astrocytomas and oligodendrogliomas showed the lowest differential count of all the tumors, coinciding directly with the relative microscopic scarcity of capillaries in these tumors.

"There was little or no concentration of dye over the site of chronic subdural hematomas, because these are relatively avascular lesions. The radiodye concentrations over large cysts are even lower than over adjacent normal brain tissue. In a cystic degenerative tumor only the actively growing tumor tissue concentrates the radiodye, whereas the cystic portions actually have a diminished uptake. In areas where the preponderance of cyst fluid over tumor cells and tumor capillaries was too great, the radiodye concentrations were not significantly increased and gave rise to most of the errors encountered with this method.

"The negative results also proved to be 95 per cent accurate and were of equal importance in the differential diagnosis of cerebral neoplasms, especially from such lesions as hypertensive cerebrovascular accidents, perichiasmal arachnoiditis, meningovascular syphilis, and intracranial aneurysms.

"Localization by the radiodye method proved to be much more precise than with electroencephalography or pneumography, whenever verification was obtained at surgery or at autopsy. Pneumography was 63 per cent focally accurate, and electroencephalography was only 45 per cent focally accurate. Tumor recurrences could be demonstrated readily with this technic. Postoperative high voltage roentgen therapy caused an increased concentration of radioactive diiodofluorescein in the more malignant intracerebral neoplasms. Special technics of counting have been evolved, so that the accuracy of localizing midline tumors, such as those of the pituitary, brain stem, or posterior fossa, is as accurate as that of localizing the more superficially situated cerebral neoplasms.

"With the apparatus and technic described above, the limitations of the test have proved to be few, provided due regard is had to accurate consistent placement of the Geiger tube on the skull and provided suspicious areas are rechecked and compared to symmetric and adjacent areas of the skull. Space-occupying lesions in every area of the skull have been localized accurately. Occasionally, localization was more diffuse, and even lateralization was difficult; in all these cases the tumor was at or near the midline or had actually crossed the midline; in several instances lesions which showed no localizing symptoms on clinical examination of the patient and in which pneumography was of no aid were accurately localized with the radiodye test, as proved at operation or autopsy.

"We believe that the radioactive diiodofluorescein tracer test is a simple, safe, painless, and reliable method for the localization and diagnosis of brain tumors, and one which should grow in value as increasingly more sensitive detection equipment and more specific radiodyes become available."

Fourteen figures, including 2 roentgenograms.

S. F. THOMAS, M.D.
Palo Alto, Calif.

Radioactive Di-iodo^{131}-Fluorescein: The Health Physics Aspect of Its Use for Diagnostic Studies. George V. LeRoy, Wilbur R. Tweedy, and Moses Ashkenazy. J. Lab. & Clin. Med. **37:** 122–128, January 1951.

Studies were conducted to determine the distribution and excretion of di-iodo^{131}-fluorescein after intravenous administration (see preceding abstract). Information was also sought on the effective half-life of the compound and the extent of the radiation hazard created by its use in diagnosis. The results are summarized as follows:

1. The effective half-life of di-iodo^{131}-fluorescein is not less than four days in man.

2. Significant concentration of the dye is found in the thyroid gland and the liver.

3. The concentration in the thyroid gland is such that a radiation dose of approximately 8.0 r may be delivered to it during the first twenty-four hours. This concentration can be reduced by the proper use of potassium iodide.

4. The urinary excretion rate is about 10 per cent on the first day, and about 1 per cent of the balance per day after that. The fecal excretion is assumed to be 10 per cent of the urinary rate.

5. The amount of radiation delivered to the total body in one week can be estimated as 0.8 r, assuming equal distribution, and the beta radiation alone from 390 μc I^{131} disintegrated in the body during that period of time.

6. The urine of patients who receive approximately 1.0 mc. as a test dose can be discharged into the sewer system without special precautions. In the case of incontinent patients, urine passed during the first twenty-four hours may contain amounts of radioactivity sufficiently large to justify the wearing of rubber gloves by attendants. In actual practice, however, no significant contamination of personnel or ward furnishings has been observed.

The authors conclude that di-iodo^{131} fluorescein, in doses of 1,000 to 1,100 μc, intravenously, can be used safely for diagnostic purposes, and that there is no significant radiation hazard to the patient or to the institution.

Seven tables.

Roentgenologic Demonstration of the Facial Nerve Canal. Marvin J. Tamari and Arthur Loewy, with the technical assistance of Eugene Elstrom. Arch. Otolaryng. **53:** 34–40, January 1951.

At the Illinois Eye and Ear Infirmary, from which this report comes, it is the practice for the otologist to make his own evaluation of roentgenograms before referring to the radiologist's report. This has led to greater interest in finer details and has encouraged correlation of clinical and roentgen findings.

It was found that the facial nerve canal was not invariably demonstrated on routine films and that increased penetration resulted in its better visualization. Studies were first made on bone specimens and then on patients, and the following technic was evolved:

The roentgenographic equipment includes a 1.0 mm. target, a rotating anode tube, a Potter-Bucky diaphragm, to absorb as much secondary radiation as possible, and a 13-cm. extension cone. The small focal spot is of the utmost importance in the portrayal of fine details. Three projections of the temporal bone are

made, with an increase over the usual kilovoltage of 6 kv., unless it is known that a destructive process exists or part of the bone has been surgically removed, in which case the increase is smaller. Thus in the Schüller-Law position, in which the routine exposure for the average skull is 56 kv. (100 ma., 1 second), 62 kv. is required for visualization of the facial canal. In the Chamberlain-Towne position the increase is from a routine 68 kv. to 74 kv., and in the Stenver position from 56 kv. to 62 or 64 kv. In the Chamberlain-Towne position the tube angle is increased from the customary 35 degrees to 45 degrees.

By this technic it is possible to visualize the course of the facial nerve canal in both sclerotic and pneumatic mastoids.

The canal is lost over the labyrinthine region of the temporal bone but is seen along the posterior aspect of the internal auditory meatus and also in its horizontal and descending portions. Changes in the canal due to tumor, cholesteatoma, granulations, and abnormality or disease during the growth period can be demonstrated. A knowledge of such changes is not only helpful in diagnosis but is also valuable in those cases where surgery is to be done. The original article should be consulted for the film reproductions showing the facial canal as demonstrated in the different projections.

Nine roentgenograms.

CORNELIUS COLANGELO, M.D.
Chicago, Ill.

Alterations in Renal Function, Including Hematuria, in Man During Intracranial Air Studies. Alterations in Cardiac Function. S. J. Weinberg, J. R. Goodman, and M. C. Bushard. Arch. Int. Med. **86:** 857–871, December 1950.

To study the effect of central nervous stimulation on renal function, ventriculography or encephalography was done in 10 patients undergoing controlled diuresis. Various tests of renal function were made and it was found that antidiuresis occurred in all 10 patients, more marked in those who had air encephalograms because of the greater irritation produced. Also noted were reduction in urinary chloride and nitrogen, hematuria, pyuria and, in one instance, albuminuria.

In 3 cases having air encephalograms, electrocardiographic changes occurred. One patient who showed cardiac arrest followed by nodal tachycardia had previously undergone ventriculography without electrocardiographic abnormalities.

Alteration of renal function following a central nervous system stimulation involves complex neuro-endocrine-vasomotor mechanisms. Nephritis, postoperative anuria, and the oliguria seen occasionally with intracranial tumors are believed to result from a central mechanism affecting renal function. Independent mechanisms are believed to exist for the control of urine volume, urinary chloride, and urea.

Five graphs; 1 electrocardiogram.

CORNELIUS COLANGELO, M.D.
Chicago, Ill.

Radiology of the Infected Temporal Bone. Harold Graham-Hodgson. Proc. Roy. Soc. Med. **43:** 989–998, December 1950.

This is an excellent concise summary covering the pathology of temporal bone infection and its radiologic study. The radiological approach here differs fundamentally from that in other skeletal disease since what is chiefly desired by the surgeon is information as to the type of petromastoid rather than as to actual evidence of infection. The first signs of infection present themselves clinically and radiologically in the eustachian tube and the middle ear. The subsequent course of the middle ear infection is very largely dependent upon the degree of pneumatization of the petromastoid bone. An early acute infection in a well pneumatized mastoid is demonstrated with ease, as any change in the radiolucency of the cells can be seen in such a case. But with poor pneumatization the radiologic interpretation becomes increasingly difficult, and with an acellular mastoid process the usual views permit no conclusion as to the presence of infection until actual bone destruction has occurred. It is in such cases that a submandibular vertical view, which reveals the path of infection, is of special value. On such a view the eustachian tube and middle ear cavity are visible and their opacity (usually resulting in invisibility) indicates infection. Thus when a mastoid is very dense and no air cells can be seen, if the eustachian tube and middle ear are clear, it is safe to assume that no acute mastoiditis is present.

So much material is presented that to abstract the article adequately is impossible. It is recommended especially to those who have entered the field of radiology since the days of sulfa drugs and penicillin.

Eleven roentgenograms. ZAC F. ENDRESS, M.D.
Pontiac, Mich.

Lateral Pharyngeal Diverticula as a Cause of Dysphagia. Jacob Buckstein and Stanley Reich. J. A. M. A. **144:** 1154–1155, Dec. 2, 1950.

Lateral pharyngeal diverticula are a rare cause of dysphagia and are not ordinarily considered in differential diagnosis. In this condition the diverticula project anterolaterally from the hypopharynx at about the level of the pyriform sinuses. In the 2 cases reported here the diverticula apparently arose from one of the embryonic pouches—either the third or fourth—incidental to the development of the branchial grooves.

The retention of food in a diverticulum causes a sense of fullness in the neck which may be relieved by emptying the sac by a change of position or lavaging it while drinking water. Regurgitated food will be found to be completely undigested. Film studies made during a barium swallow demonstrate the diverticula projecting at the level of the hypopharynx.

Six roentgenograms. ALFRED O. MILLER, M.D.
Louisivlle, Ky.

Adamantinomas. Carman Weder. Canad. M. A. J. **63:** 590–594, December 1950.

Among 26,366 cases in the files of the Saskatchewan Cancer Clinics, only 8, or 0.07 per cent, were diagnosed as adamantinoma. Though 85 per cent of these tumors occur in the lower jaw according to the general literature, in this series there was an equal division between the lower jaw and the antrum.

The lesion presents itself usually as a slow-growing painless lump causing the facial contour to bulge outwardly. The swelling may extend inwardly, producing difficulty in swallowing. Involvement of the maxilla may cause obstruction of the nares. The swelling may be hard, or there may be soft fluctuant areas. The overlying skin is movable unless fixed by a superadded inflammatory ulcer or sinus.

The tumors may be solid or cystic, and combinations of the two forms are seen. Metastasis is infrequent, though McGregor (Acta radiol. **16**: 254, 1935) has collected 10 cases with secondary involvement of the lymph nodes and lungs. Radiologically the main feature is a centrally expanding tumor, causing bulging of the overlying periosteum. The margins are clear and may show some sclerosis.

Radical surgery is the treatment of choice. Radical irradiation may have a place in certain cases.

Histories of 7 of the cases, all proved histologically, are included.

Three roentgenograms; 1 photomicrograph.

JOHN M. KOHL, M.D.
Jefferson Medical College

THE CHEST

Topographical Visualization of the Bronchial Tree in the Roentgenogram. Paul Ch. Schmid. Fortschr. a. d. Geb. d. Röntgenstrahlen **73**: 307–317, July 1950. (In German)

Heretofore it has been deemed sufficient to localize pathological pulmonary processes according to the lobe involved. Because of the advance in lung surgery this is no longer adequate. Certain portions of each lobe belong to a primary and secondary bronchus. This paper deals with the topographical anatomy of these important lung structures as they appear on the bronchogram.

On the basis of 300 of his own cases, the author arrives at the following conclusions: There are 4 main bronchial branches, or primary bronchi, as shown by bronchography: the upper lobe bronchus, the middle lobe bronchus, the lingular bronchus, and the lower lobe bronchus. Each of the primary bronchi has two or more secondary bronchi, which are described and illustrated in detail. The upper lobe bronchus has three secondary bronchi: an apical, a posterior, and a cardiac branch. The middle lobe bronchus has two branches: a lateral and a medial secondary bronchus. The lingular bronchus has also two secondary bronchi: a superior and an inferior branch. The lower lobe bronchus has five secondary bronchi: apical, cardiac, ventral, axillary, and dorsal.

This paper is well illustrated, and detailed information should be obtained from the original.

Twelve drawings; 5 photographs.

EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

Topographical Visualization of the Lung Segments in the Roentgenogram. Paul Ch. Schmid. Fortschr. a. d. Geb. d. Röntgenstrahlen **73**: 318–332, July 1950. (In German)

A lung segment is that portion of a lung (lung unit) which is supplied by a primary bronchus, one artery, and two pulmonary veins. It is of an irregular cone shape or a regular pyramid shape, the tip always pointing toward the hilus, the base toward the periphery. It is generally believed that the lung segment has also an independent nerve supply.

The author's observations are based upon some 20,000 roentgenograms of children. A large number of schematic drawings illustrate the various primary and secondary lung segments. The study was done chiefly on cases of infantile tuberculosis with benign infiltration, atelectasis, and shrinking of certain lung segments.

Fifty-five drawings.

EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

A Water-Soluble Contrast Medium for Bronchography. Report on Clinical Use. Robert J. Atwell and Robert L. Pedersen. Dis. of Chest **18**: 535–541, December 1950.

Viscous umbradil, a water-soluble contrast medium, was first described by Morales and Heiwinkel (Acta radiol. **30**: 257, 1948. Abst. in Radiology **53**: 303, 1949), and further studies on its application were reported by Morales (Acta radiol. **32**: 317, 1949. Abst. in Radiology **55**: 465, 1950). The authors of this paper have used a similar preparation—viscous umbradil B—for bronchography with excellent results. This consists of umbradil (diodrast) 50 per cent, sodium carboxymethylcellulose (CMO^R) 3.3 per cent, and xylocaine, a local anesthetic, 0.5 per cent.

The technic of injection is the same as that of the oily media. The authors prepared their patients by giving them nembutal, codeine, and atropine. The pharynx, larynx, and vocal cords were anesthetized by 1 per cent pontocaine and the same solution was instilled through a small rubber catheter introduced by way of the nose, for anesthetization of the trachea and bronchi. A total of about 6 c.c. proved sufficient. The viscous umbradil mixture is also instilled through the catheter, the patient being positioned in accordance with the lobe, or lobes, to be examined. About 10 to 15 c.c. are needed for each lung. Exposures are made at a tube-to-film distance of 66 inches and about 5 kv. are added to the exposures for normal chest films in various positions. Speed in the examination is essential, for there is a tendency for the material to flow from the upper into the lower lobes. The bronchograms are diagnostic, and examinations made five hours after the instillation of the medium show no residue.

No untoward effects have been observed with this medium. Contraindications to its use are acute respiratory infection, acute nephritis or uremia (since excretion is by way of the kidney), and sensitivity to umbradil (rare). The authors believe it has many advantages over iodized oil.

Six roentgenograms. HENRY K. TAYLOR, M.D.
New York, N. Y.

Bronchography with Joduron B, a Water-Soluble Contrast Medium. Carmelo Scarinci. Radiol. med. (Milan) **36**: 998–1003, December 1950. (In Italian)

Joduron B is a viscous, water-soluble, stable preparation containing iodine, of a specific gravity of 1.29 and a viscosity of 11,000 (Hoppler) at 20° C. This substance is readily absorbed by the bronchial mucosa, and three or four hours following the injection no residual shadows can be seen in the roentgenograms of the lungs. The preparation is somewhat more irritating than lipiodol, so that the patients will cough a little more after the intratracheal injection unless the anesthesia has been carried through a bit more deeply than is usual with iodized oil. Joduron B has been used with good results by Fischer of Zurich (Schweiz med. Wchnschr. **78**: 1025, 1033, 1948. Abst. in Radiology **53**: 440, 1949). Scarinci reports his own experience and shows 15 excellent roentgenograms.

The advantages of a water-soluble preparation are

self-evident, and this work should be followed with interest by all those interested in bronchography.

CESARE GIANTURCO, M.D.
Urbana, Ill.

Routine Antenatal Chest X-Ray Findings in Patients Drawn from a Currently Surveyed Population. Hugh J. Bickerstaff, George W. Comstock, and Mary H. Burke. Am. J. Obst. & Gynec. **61**: 41–48, January 1951.

The study reported here was performed in a county (Muscogee County, Georgia) with a total population of almost 100,000 people, in which a rather thorough photofluorographic chest survey for tuberculosis had been done. An estimated 85 per cent of all women in the childbearing ages (15 to 44 years) had been covered in three years by the tuberculosis survey.

Working with this group of people, the authors have been securing additional routine microfilms of the chest of all patients on the first day of attendance at the prenatal clinic. Such films were obtained in 3,576 pregnancies. Four per cent of the patients showed abnormalities sufficient to warrant further clinical investigation. Thirty-seven women were suspected of having tuberculosis, and in 14 the disease proved to be active. Nine cases were first discovered by the prenatal microfilm examination, and 3 of these were definitely active.

Thirty cases of clinically important non-tuberculous pathologic conditions were also found by the prenatal survey. These were chiefly cardiovascular.

In addition to the above findings, 10 cases of pulmonary tuberculosis were found post partum by microfilm survey. Five of these women had had prenatal microfilms interpreted as negative, and the other 5 had not been examined before childbirth.

The authors conclude that their findings indicate the value of routine prenatal x-ray examination of the chest. They suggest that an additional routine postpartum film would probably be worth while in finding tuberculosis in women of the childbearing age.

Eight tables. T. FREDERICK WEILAND, M.D.
Jefferson Medical College

Value of a Total Population Roentgen Chest Survey in the Campaign against Tuberculosis. Lars Lönnerblad. Acta radiol. **34**: 501–516, December 1950.

Two paramount reasons are advanced which show the impossibility of isolating effectively all tuberculous individuals: (1) The disease is usually of insidious onset and long duration and does not always entail inability to work. (2) The tuberculous process may become rapidly progressive in a lung which a short time before was considered healthy or at least free from active disease. Cases illustrative of both situations are presented.

The prognosis in pulmonary tuberculosis is not easy to predict. A certain percentage of people develop *clinical tuberculosis* for reasons which are not at all clear. The mortality in these so-called "open" lesions is equal to that of cancer. They defy all therapeutic measures.

Prediction of therapeutic results is a very complicated problem and one essentially unsolved. Tuberculosis mortality statistics in Sweden showed a decline subsequent to 1900 and before any medical measures of effective nature were developed. The decline there has been steady and apparently unrelated to the latest therapeutic advances.

During 1943, 99 per cent of the population over one year of age in Gotland, a remote island off the mainland of Sweden, was photofluorographed. Mortality statistics there in the subsequent years have not dropped any more than in the remainder of Sweden. Consequently it is felt that the survey was productive of no appreciable results.

It is obvious, says the author, that photofluoroscopy is of importance when a large special group of persons must be segregated in barracks or educational establishments, since under these circumstances carriers of infection can be separated fairly effectively, but without more economic aid to persons with tuberculosis and to susceptible groups, and without widespread BCG inoculation, total population surveys can hardly produce the desired results.

Twelve roentgenograms. Two graphs.

JOHN F. RIESSER, M.D.
The Henry Ford Hospital

Results of Chest X-Ray Screening in Hospitals. John E. Madden. Illinois M. J. **98**: 354–356, December 1950.

This article describes in detail the method used for chest surveys in three hospitals in Decatur, Ill. It is of interest to note that only 50 per cent of the patients admitted to the hospitals were examined. The remainder represented emergencies, or were discharged or admitted over a weekend, and were thus never sent to the photoroentgen unit for examination.

S. F. THOMAS, M.D.
Palo Alto, Calif.

Miniature Radiography with 4 × 5 Inch Cut Film. Owen Clarke. Lancet **2**: 757–759, Dec. 9, 1950.

In Great Britain only 35-mm. roll film has so far been obtainable for miniature radiography, and all attention has been focused on mass surveys. The author believes that the use of miniature photofluorography for general radiological purposes in hospitals and clinics should now be considered. Except for survey work, he thinks the 4 × 5-inch cut film is preferable to roll film for photofluorography, and that it has many advantages over full-size film for clinical purposes. The author's experience is based on 25,000 x-ray films taken for the Ontario Immigration Department in London in 1948–49.

One roentgenogram.

Cardiological Case Finding by Means of Mass Miniature Radiography. Peter O. Leggat. Brit. M. J. **2**: 1364–1366, Dec. 16, 1950.

The results of two mass chest surveys, one industrial and one in a mental institution, are analyzed in respect to cardiac case finding. In the two surveys, covering 12,173 subjects, 47 cases of cardiac disease were diagnosed radiologically and checked by clinical observation. Of the cases thus diagnosed in the industrial group, totaling 44, 24 had been previously recognized. In the mental hospital group (244 subjects), only 3 cases were diagnosed radiologically out of a known total of 15. On this basis, the author concludes that miniature radiography is of value in detecting some cases of cardiac disease but that many cases will be missed for technical reasons or because no x-ray changes are present.

Two graphs; 1 table. ZAC F. ENDRESS, M.D.
Pontiac, Mich.

Bronchopulmonary Hypogenesis: Diagnosis in the Living. Isadore Meschan and Joseph D. Calhoun. South. M. J. **43:** 1038–1042, December 1950.

Bronchopulmonary hypogenesis may be defined as the incomplete development of a variable segment of bronchus or pulmonary tissue. The authors report a case involving the right middle and lower lobe bronchi. This is believed to be the sixth reported case of this anomaly diagnosed before death and is particularly significant in that the abnormality was first discovered on a 70-mm. microfilm during a chest survey. The patient was transferred to a tuberculosis sanitarium for several months and was regarded as having either tuberculosis or carcinoma of the lung. He was then admitted to the University of Arkansas Hospital, where he underwent a thorough work-up which revealed the true nature of the anomaly. The patient was still living at the time of the report but the diagnosis was held to be established beyond question by bronchography and bronchoscopy. There was associated herniation of the ascending colon, hepatic flexure, appendix, and terminal ileum into the right chest.

Clinically bronchopulmonary hypogenesis is usually relatively asymptomatic. Upon physical examination, the heart and mediastinum are usually found shifted to the affected side, with hyperresonance on the opposite side. There are frequently other associated anomalies. Burger, in a review of 54 collected cases (Am. J. Dis. Child. **73:** 481, 1947. Abst. in Radiology **50:** 257, 1948), found this condition more frequently on the left side.

The authors point out that bronchopulmonary hypogenesis will be found with increasing frequency among the relatively asymptomatic population as chest surveys become more popular.

Four roentgenograms.

ROBERT H. LEAMING, M.D.
Jefferson Medical College

Relation of Tracheotomy and Laryngeal Carcinoma to Pulmonary Tuberculosis. Alvin D. Rudo and David H. Jones. Ann. Otol., Rhin. & Laryng. **59:** 931–942, December 1950.

Whether tracheotomy and laryngeal carcinoma bear any relationship to the activation of pulmonary tuberculosis is a matter of controversy. The authors' contribution to the question is based upon 43 patients undergoing tracheotomy and 79 patients with carcinoma of the larynx, seen over a three-year period. Twenty-nine of the patients with carcinoma were treated by laryngectomy; the remainder received no treatment. A diagnosis of pulmonary tuberculosis was made in 10 of the patients under observation; 4 of these had no active lesions prior to treatment. In 3 the underlying disease was aggravated, while only 1 patient was unaffected by therapy.

The authors' cases were of two types: Type A, in which tracheotomy and laryngeal cancer apparently awakened inactive or primary complex pulmonary tuberculosis (4 cases); Type B, in which irradiation of laryngeal cancer affected an active pulmonary infection (6 cases).

From their observations the authors are inclined to the view that laryngeal cancer exerts a deleterious effect on pulmonary tuberculosis. The nature of the relationship of the two diseases is discussed at length, but no very definite conclusions are reached.

Intercurrent infection is assumed to play a major role in the pathogenesis of tuberculosis, and this could be a factor in tracheotomy cases, where secondary bronchitis and susceptibility to upper respiratory disease are produced. Trauma also has a definite place in the activation and progression of tuberculosis. The effect of radiation therapy may also be accepted as a factor. It is known that irradiation of the lung can easily activate latent or inactive tuberculosis. Whether localized laryngeal radiation has a direct or an indirect effect is, of course, purely conjectural.

It has been stated (Parke, Loftus, and Bishop: New York State J. Med. **48:** 1685, 1948) that patients who have had thoracic surgical operations have a wider spread of tuberculosis due to over-medication preoperatively, with loss of cough reflex. This might occur following laryngeal and neck surgery for cancer.

The wearing of a cannula causes an unnatural inspiration of air which has not yet been previously warmed, moistened, and filtered; thus such cold and dust-laden air may damage the lower air passages and lungs, and contribute to the development of bronchopulmonary tuberculosis.

It is recommended that laryngeal cancer patients be closely watched before and after treatment for signs of pulmonary tuberculosis. Where both conditions are present, immediate attention should be directed to the tuberculous process.

Six roentgenograms. STEPHEN N. TAGER, M.D.
Evansville, Ind.

Clinical Variations in Primary Atypical Pneumonia. William S. Jordan, Jr., Robert W. Albright, French H. McCain, and John H. Dingle. Am. J. Med. **10:** 3–20, January 1951.

A review of 67 cases of primary atypical pneumonia observed in a general hospital emphasizes the variety of clinical patterns attributable to this disease. The illnesses ranged in severity from an obscure fever to a severe pulmonary infection with circulatory collapse. Not only did this syndrome mimic tuberculosis and other forms of pneumonia but, particularly in older individuals, it was confused also with cardiac decompensation, emphysema, and chronic bronchitis associated with other febrile illnesses.

Four types of roentgenographic picture are defined, as follows: (1) Bronchitic: increased size and density of one or both hilar shadows with prominent bronchovascular shadows extending out from the hilus. (2) Peribronchitic: prominent bronchovascular markings extending from the hilus into the cardiophrenic sinuses and outward into the lung, together with peribronchial infiltration which still allowed the linear markings to be clearly visible through the infiltration. (3) Alveolar: dense infiltration which obscured the peribronchial markings in its central portion. The size, shape, location, and degree of density were variable. (4) Lobar: dense consolidation suggesting a lobar type of consolidation. The incidence of the four types was: bronchitic, 40 cases; peribronchitic, 41 cases; alveolar, 31 cases; lobar, 7 cases. While the mildest form, bronchitic, was common, in only 5 cases was it the sole type present throughout the course. One-half of the cases progressed to the alveolar form with easily recognizable consolidation.

On admission, 50 per cent of the cases had pulmonary signs which corresponded in extent with the amount of infiltration shown by roentgenograms. The other 50 per cent showed discrepancies between signs and roentgeno-

grams, almost as many patients exhibiting predominance of signs as exhibited predominance of infiltration roentgenographically. In 10 cases the correlation between physical findings and roentgenographic changes remained poor throughout the illness, and in most of these cases the signs spread widely while the roentgen picture remained unchanged. The average duration of abnormal pulmonary signs after onset was three weeks, but 15 per cent of the patients had such signs for more than four weeks.

The level of the leukocyte count on admission was related to the duration of disease. Two-thirds of the patients had counts below 9,000 on admission; two thirds had counts over 9,000 during hospitalization. An increase in leukocyte count most often accompanied spread of the pulmonary lesion.

Fourfold or greater rises in titer, either of cold hemagglutinins or streptococcal MG agglutinins, or both, occurred in 43 cases, in direct correlation with the severity of the illness.

Seven charts; 8 tables.

The Blood Flow Through an Atelectatic Lung. Viking Olov Björk and Ernst F. Salén. J. Thoracic Surg. **20**: 933–942, December 1950.

Experimental atelectasis was produced in dogs and, with the aid of an opaque medium, observations were made on the flow of blood through the atelectatic lung and the contralateral expanded lung. In acute atelectasis angiocardiography showed no decrease in the size of the pulmonary arteries and the capillary bed was found to remain open as indicated by the contrast filling of pulmonary arteries and veins simultaneously on both sides. In chronic atelectasis, interval studies demonstrated gradually decreasing circulation in the collapsed lung during the first month, until practically no blood was passing through the non-ventilated areas. After the first month, opaque medium was observed to linger in the arterial phase on the affected side, while the veins showed dye earlier on the expanded side. The blood, therefore, was believed to fill out the arteries of the atelectatic lung but to pass either not at all, or extremely slowly, through the capillary bed. The capillaries appeared to be closed down, somewhat as in a resting part of an organ. No decrease in size of the pulmonary artery to the atelectatic lung was noted until the collapse had been maintained several months.

These observations were checked chemically by measurement of arterial oxygen saturation. With unilateral, complete atelectasis in a dog breathing pure oxygen, arterial oxygen saturation was roughly 90 per cent. This was just about the same result as that obtained by arranging apparatus so that one fully expanded lung breathed pure oxygen while the other fully expanded lung breathed pure nitrogen. Therefore, the arterial oxygen deficit in acute atelectasis is directly attributable to the continued normal volume of blood flow through the non-functioning atelectatic lung. The large volume of non-oxygenated blood mixes with refreshed blood from the contralateral, functioning lung. Follow-up studies at intervals of days, weeks, and months demonstrate a progressive increase in arterial oxygen saturation. This corresponds with decreased blood flow through the atelectatic lung as demonstrated with radiopaque medium.

Nine roentgenograms.

DONALD DEF. BAUER, M.D.
St. Paul, Minn.

Unusual Conditions Simulating Pulmonary Atelectasis, with Case Reports of Agenesis and Hypoplasia of the Lung and of Fracture of the Bronchus, Together with Report of a Case of Massive Atelectasis in Bronchial Asthma Included for Comparison. Robert E. Priest. Ann. Otol., Rhin. & Laryng. **59**: 889–907, December 1950.

Some unusual cases in which an initial or "working" diagnosis of pulmonary atelectasis proved to be incorrect are presented. Included are cases of idiopathic pulmonary hypoplasia, pulmonary hypoplasia associated with congenital heart disease, pulmonary hypoplasia accompanying diaphragmatic hernia, unilateral pulmonary agenesis, and traumatic bronchial rupture. A case of total pulmonary atelectasis due to bronchial asthma is included for comparison. Bronchoscopy was of material assistance in the diagnosis of all these cases, and bronchography was helpful in some.

Thirteen roentgenograms; 1 photograph.

STEPHEN N. TAGER, M.D.
Evansville, Ind.

Spontaneous Pneumothorax—Contrast of the Benign Idiopathic and the Tuberculous Types. Bernard Hyde and LeRoy Hyde. Ann. Int. Med. **33**: 1373–1377, December 1950.

It is important to differentiate spontaneous pneumothorax caused by tuberculosis from that occurring in the absence of disease, because of the great differences in treatment and prognosis. At the Birmingham Veterans Administration Hospital, in a two-year period, 41 cases of benign idiopathic spontaneous pneumothorax and only 10 cases of tuberculous spontaneous pneumothorax were seen. The present paper is based on 76 cases of the benign idiopathic type and 35 associated with tuberculosis.

The radiological and clinical differences between the two types are summarized in the following table:

	Benign Idiopathic Spontaneous Pneumothorax [76 cases]	Tuberculous Spontaneous Pneumothorax [35 cases]
1. Pulmonary infiltration on chest x-ray	0%	0%
2. Pleural adhesions	0%	91%
3. Pleural fluid above level of diaphragm	5% (these 4 patients had grossly bloody fluid)	54%
4. Immediate hospital mortality rate	0%	29%
5. Clinically ill	Not usually, and only very briefly (1–2 days)	Almost always
6. Fever present	If present, for only a few days, never more than 7 days, and low-grade (99–100°)	Commonly. Usually prolonged, and level may be higher (above 100°)
7. After-care required	None. Patient can return to full activity after collapsed lung has reexpanded	Continued bed rest and treatment of pulmonary tuberculosis

STEPHEN N. TAGER, M.D.
Evansville, Ind.

Right-Sided Spontaneous Pneumothorax Complicating Therapeutic Pneumoperitoneum. Joseph Ross and Jason E. Farber. Am. Rev. Tuberc. **63**: 67–75, January 1951.

This report is concerned only with cases of spontaneous pneumothorax complicating pneumoperitoneum in which there is simultaneous disappearance of the gas in the abdomen. Although this syndrome has been infrequently recorded, the authors have seen 3 cases and cite 12 more which were reported to them in answer to a questionnaire sent to a group of California chest physicians. In all, the pneumothorax was right-sided.

The hypothesis that air from the peritoneum follows along the connective-tissue sheath of the esophagus and great vessels into the mediastinum and from there enters the thorax *via* a rent in the pleura, due to the increasing pressure, is not tenable, for there was no definite evidence of mediastinal emphysema in the recorded cases and, furthermore, spontaneous pneumothorax associated with mediastinal emphysema is almost always left-sided. A second concept, which the authors feel is the more likely, is that a defect in the diaphragm allows the air to enter the thorax.

Congenital defects in the diaphragm are more common on the left side than on the right, but they are likely to be large and to result in herniation of abdominal contents into the thorax early in life, with no hernial sac of peritoneum. Hernias through the foramen of Morgagni have a hernial sac and are commonly right-sided. In addition, this area is normally protected by the liver. When pneumoperitoneum is instituted, however, this protection is lost, and the defect, if present, is subjected to all changes in intraperitoneal pressure. The same is true of defects or weak areas elsewhere in the right diaphragm. Localized atrophy of the diaphragm is reported to follow therapeutic phrenic paralysis, and blebs have been noted on the upper surface of the diaphragm in patients with paralyzed diaphragms who were receiving pneumoperitoneum and pneumothorax concurrently.

The combination of a defect in the diaphragm, either congenital or acquired, with the unusual stress brought to bear upon it in pneumoperitoneum, which separates the diaphragm and the liver, is felt to be the cause of pneumothorax in these cases. The size of the diphragmatic defect probably has a bearing on the temporal relationship of this complication to the initiation of the pneumoperitoneum. In general, the larger the defect, the sooner pneumothorax appears; unusual stress with marked increase in intra-abdominal pressure is probably necessary to produce pneumothorax in cases with small or potential defects.

Eight roentgenograms; 1 table.

JOHN H. JUHL, M.D.
University of Wisconsin

The Radiologist's Responsibility in Bronchogenic Cancer. A. C. Singleton. J. Canad. Assoc. Radiologists **1**: 59–68, December 1950.

The radiologist must accept a large part of the responsibility in the diagnosis of early bronchogenic cancer since the history and physical examination may be negative or misleading. He must regard with suspicion all slowly resolving or recurring inflammatory lesions, and even small peripheral lesions which do not clear rapidly, and must be prepared to conduct further investigations by laminagraphy or bronchography, or both, when any doubt exists. These special procedures are of particular value in upper lobe and peripheral lesions, a group constituting some 25 to 40 per cent of pulmonary cancers and one in which bronchoscopy is negative.

Probably the most important roentgen sign of bronchogenic cancer is atelectasis, lobar or lobular. The classical signs of mediastinal shift, narrowing of the interspaces, and elevation of the diaphragm, are easily seen, but the position of the hilus and interlobar fissures and the spacing of the lung markings must be carefully studied. Laminagraphy will not infrequently reveal cavitation in lesions in which it was previously unsuspected, and may show tortuous or irregular bronchial filling defects which are characteristic of carcinoma. It is also frequently possible to demonstrate complete bronchial occlusion by this means. Bronchography is one of the most useful procedures available for determining the character of pulmonary densities and their bronchial or extra-bronchial location.

In chest surveys the possibility of cancer must always be kept in mind. Age and the presence of other diseases of known etiology do not exclude a diagnosis of bronchogenic cancer.

Six cases illustrate the author's main points.

Seventeen roentgenograms.

ZAC F. ENDRESS, M.D.
Pontiac, Mich.

Alveolar Cell Tumor of the Lung. Martin W. Davis and Thomas R. Simon. Am. Rev. Tuberc. **62**: 594–609, December 1950.

Five cases of alveolar-cell tumor of the lung are presented, and the clinical and pathologic features are discussed. All of the patients were women. The average age was seventy-two and the average duration of life from the onset of symptoms was fifteen months.

The principal symptoms were dyspnea, cough, and expectoration of moderate amounts of whitish foamy or mucoid material, pleuritic chest pain, and weight loss. The physical findings included cyanosis, tachypnea, and low-grade fever. Alterations in breath sounds or percussion note, together with râles on both sides of the chest, were usually observed. Laboratory studies revealed a mild anemia and an elevated leukocyte count with a shift to the left in the differential count in 3 of the 5 cases. Examinations of the sputum were entirely negative, but in only 1 patient was the sputum examined for malignant cells.

Roentgen examination of the chest gave definite positive findings in every instance. Infiltration in the lung fields was demonstrated in each case, bilateral in all but one. The infiltrations were variously described as diffuse, fibrotic, mottled, nodular, conglomerate, and feathery. The findings were most frequently misinterpreted as tuberculosis or primary atypical pneumonia, the former being ruled out by the absence of tubercle bacilli in the sputum and the latter by the protracted downhill course.

Therapeutic measures were of little apparent benefit. Oxygen therapy seemed to be of only temporary value in prolonging life. Aminophylline given intravenously appeared to be of some benefit for the severe terminal dyspnea in one patient.

At present the only exact method of diagnosis of alveolar-cell tumor is by thoracotomy and removal of a biopsy specimen for microscopic examination.

Four roentgenograms; 5 photomicrographs.

Pulmonary Infiltration and Blood Eosinophilia in Children (Loeffler's Syndrome). A Review with Report of Eight Cases. Rosa Lee Nemir, Arthur Heyman, J. D. Gorvoy, and Edmund N. Ervin. J. Pediat. **37:** 819–843, December 1950.

Eight cases of pulmonary infiltration and eosinophilia in children are reported. All but one of the patients were Puerto Ricans living in New York City. Five of the cases were mild and corresponded to the original description of Loeffler's syndrome. The other 3 cases illustrate the chronicity of the condition. Fine mottling throughout the lung fields simulating miliary tuberculosis was seen in roentgenograms of these 3 patients. In 2 cases the shadows persisted for seven and one-half months and in the other for seven weeks. In 7 cases the pulmonary shadows cleared before the eosinophil count returned to a normal level.

In 7 patients intestinal parasitism was found. In the eighth patient, bacterial allergy associated with infected sinuses is suggested as the cause of the Loeffler's syndrome.

Five roentgenograms; 4 tables.

Results of Histoplasmin Skin Testing in Children from the St. Louis, Mo., Area. John F. Lynch and E. Bryce Alpern. J. Pediat. **38:** 51–54, January 1951.

Between November 1946 and May 1947, 500 children in the St. Louis area were tested intradermally with histoplasmin. There was no selection of subjects with regard to diagnosis, race, or sex. Special attention was given to children under three years of age, and this age group comprises the majority of patients studied. Seventy-three children (14.6 per cent) gave positive reactions to histoplasmin, and the incidence of positive tests was found to increase rapidly up to the age of ten.

Of 362 children under three years of age, only 5 were found to be histoplasmin-positive. The youngest of these was four and a half months of age. Roentgen examination of the chests of these 5 patients revealed no evidence of calcification.

The geographic location of the homes of the last 43 patients with positive histoplasmin reactions was determined: 30 lived in a rural area or in a community of less than 5,000 people.

Chest roentgenograms were available for 18 children who had reacted positively to histoplasmin. In 9 children there was calcification of the tracheobronchial lymph nodes as well as the parenchyma, and peritracheal and hilar lymphadenopathy was present in 5. Findings were normal in the remaining 4 cases. None of this group of 18 had a positive tuberculin test.

A high incidence of chronic disease among positive histoplasmin reactors was noted.

Four tables; 1 graph.

The Kartagener Syndrome. Samuel Cohen, Joseph D. Goldstein, and John Hamill. J. M. Soc. New Jersey **47:** 557–560, December 1950.

The authors present the case report of a patient with the "Kartagener triad," consisting of sinusitis, bronchiectasis, and complete transposition of the viscera. Roentgenograms in 1934, at the age of five, demonstrated transposition of the viscera and enhanced bronchovascular markings in both lung fields. Subsequent films in 1948 and 1949 showed a similar picture. Bronchography in the latter year revealed evidence of cylindrical bronchiectasis in portions of both lower lobes and in the left middle lobe. Examination of the sinuses showed small frontal cells, poorly developed sphenoidal cells, and considerable loss of aeration in the ethmoidal cells and antra.

The authors call attention to the unusually high incidence of bronchiectasis in patients with situs inversus (from 16 to 23 per cent). The possible pathogenesis of the triad is discussed, as well as the relation of the bronchiectasis to the situs inversus. Presence of multiple congenital aberrations has been suggested, with the basic abnormality possibly an altered secretory activity of the mucosa of the respiratory tract. A definite statement as to the pathogenesis is not made.

Six roentgenograms.

HARRY FLAX, M.D.
University of Louisville

Pulmonary Changes in Uremia. Hyman E. Bass and Emanuel Singer. J. A. M. A. **144:** 819–823, Nov. 4, 1950.

The authors review the literature correlating the clinical, roentgenographic and pathologic pulmonary changes in uremia, pointing out that fresh areas of pneumonia and older areas of bronchiolitis obliterans were noted by Ehrich and McIntosh (Arch. Path. **13:** 69, 1932), and increased densities confined to the hilus and inner lung zones by Roubier and Plauchu (Arch. méd. chir. de l'app. respir. **9:** 189, 1934). Rendich, Levy, and Cove (Am. J. Roentgenol. **46:** 802, 1941. Abst. in Radiology **39:** 114, 1942) considered the pulmonary changes to be related to left ventricular failure. Dock (J. A. M. A. **125:** 1083, 1944) believed that the associated air hunger was responsible for the maintenance of distention of peripheral alveoli. Doniach (Am. J. Roentgenol. **58:** 620, 1947. Abst. in Radiology **51:** 436, 1948) reported no correlation of the roentgen appearance of the lung with blood urea levels. Barden and Cooper (Radiology **51:** 44, 1948) included uremic pneumonia as one of the conditions associated with increased vascular permeability of the lung.

Five cases are reported, 1 of which had no x-ray examination, and only 2 of which had serial roentgen observations. Three of the 5 patients had associated hypertensive heart disease and were in varying degrees of failure. The remaining 2 had arteriosclerotic heart disease. The 2 cases followed with serial x-rays were in the hypertensive group, and the extensive hilar and inner lung field shadows cleared remarkably with alleviation of left ventricular failure. The x-ray changes are attributed to altered permeability of congested alveolar capillaries as a result of left ventricular failure, with sparing of the periphery due to its more extensive motion, as suggested by Dock. Of the 4 cases coming to autopsy, all showed "fibrinous alveolitis" of varying degrees with thickening of the alveolar septum. Congestive changes of the alveolar capillaries were noted in 2 cases. Hyaline changes in the alveolar septum and in the intra-alveolar exudate were also observed in 2 cases.

Three roentgenograms; 2 photomicrographs.

WALTER M. WHITEHOUSE, M.D.
University of Michigan

A Fatal Case of Pneumomediastinum, Subcutaneous Emphysema, and Pneumothorax Lenta in a Newborn Infant. John A. Ripp. J. Pediat. **37:** 917–921, December 1950.

A fatal case of pneumomediastinum, subcutaneous emphysema, and pneumothorax complicated by pul-

monary hemorrhage and infection, presenting the classical clinical and roentgenologic picture, is reported because of its interesting course and pulmonary pathology. The necropsy findings are described.

A review of the literature reveals this to be a comparatively rare condition, but it should be considered in the differential diagnosis of respiratory distress in a newborn infant.

Four roentgenograms.

Management of Aspirated Straight Pins in the Bronchi Utilizing the Stereoscopic Fluoroscope. Alden H. Miller. Arch. Otolaryng. **53**: 68–76, January 1951.

Straight pins aspirated into the bronchi should be removed when possible by direct or blind grasping with a forceps under bronchoscopic guidance. Should this fail, as happens when the pin is in a terminal bronchus, stereoscopic fluoroscopy to direct the bronchoscope to the foreign body is usually successful. Roentgenographic demonstration of the pin near the lung perimeter usually suggests the need for stereoscopic fluoroscopy, since the pin is probably in a terminal bronchus.

The stereoscopic fluoroscope permits three-dimensional vision. It can be operated in the upright or horizontal position and is believed to offer definite advantages over the biplane fluoroscope. The foreign body seems to move about widely until the forceps enters the correct bronchus; it then becomes stationary.

The roentgen dose to the patient's skin is indicated by a cumulative timer. In one of the cases presented it was only 31 r.

When all methods of removal, including the use of a pin-bending forceps fail, early transpleural removal should be done.

Six roentgenograms; 2 photographs.

CORNELIUS COLANGELO, M.D.
Chicago, Ill.

Electrokymography: A Preliminary Report. R. J. Tahan and S. F. Oosthuizen. South African M. J. **24**: 1081–1084, Dec. 30, 1950.

The authors follow the technic of Henny and Boone for electrokymography (Am. J. Roentgenol. **54**: 217, 1945; **57**: 409, 1947. Abst. in Radiology **47**: 88, 1946; **50**: 848, 1948), the only difference being that, instead of timing the phases of the electrokymograms by the carotid pulse, they use a phonocardiogram.

The article covers the usage of the electrokymograph, with sample tracings of the normal wave outlines, compares the instrument with a standard kymograph, and speculates on its possible uses as an aid in the diagnosis of myocardial infarction and of doubtful cases of mitral incompetence. Its physiological usefulness is self-evident.

Three illustrations. S. F. THOMAS, M.D.
Palo Alto, Calif.

Simultaneous Angiocardiotomography. B. Lindemann. Fortschr. a. d. Geb. d. Röntgenstrahlen **73**: 261–267, July 1950. (In German)

Visualization of pathological conditions of the heart and blood vessels has become more and more important owing to the great advance in heart surgery. Angiocardiography was the first step toward a better diagnosis, permitting visualization of the blood vessels and the chambers of the heart. Many diagnostic problems, however, are still unsolved in spite of technical advances.

Congenital heart failure is often combined with various malformations of the septum. In ordinary angiocardiograms the different portions of the heart are superimposed and a correct diagnosis is almost impossible. Pulmonary stenosis, in which the obstruction lies below the valve, likewise cannot be recognized accurately by ordinary methods.

To insure greater accuracy in the diagnosis of septal defects and other congenital heart diseases, Lindemann recommends the simultaneous use of angiocardiography and planigraphy. The focus target distance remains fixed and four roentgenograms are taken at the same exposure, with films 1.4 cm. apart. Four different types of intensifying screens are used to obtain the highest possible degree of contrast.

To illustrate the technic the author shows roentgenograms of a heart specimen filled with barium-paraffin. No clinical cases are cited.

Seven roentgenograms; 3 diagrams.

EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

On Congenital and Positional Anomalies of the Aorta. Hans Franke. Fortschr. a. d. Geb. d. Röntgenstrahlen **73**: 267–280, July 1950. (In German)

Clinically insignificant abnormalities are often misinterpreted. With the present progress in the diagnosis of pathological conditions of the heart and large blood vessels, one should be aware of the many anomalies which may occur.

Eight different types of congenital anomalies of the aorta are discussed in detail and the following classification is presented:

1. Simple upper displacement of the arch of the aorta to the right—*arcus aortae dexter simplex.*
2. Upper and right displacement of the arch of the aorta, "encircling" type—*arcus aortae circumflexus.*
3. Marked upper and right displacement of the arch with the aorta crossing behind the esophagus to the left side in the middle and lower portion—*arcus aortae dexter* and *decussatio sinister.*
4. Upper and right displacement with obliteration of the left aortic arch—*arcus aortae duplex incompletus.*
5. Double aortic arch—*arcus aortae duplex completus.*
6. Absent aortic arch—*arcus aplasia* or, in some cases, *arcus hypoplasia.*
7. *Arcus aortae dexter* with low position of the pulmonary artery.
8. *Arcus aortae dexter* with atresia of the pulmonary artery.

A right-sided arch forms one element in both the Eisenmenger complex and the tetralogy of Fallot.

Among the positional anomalies two conditions are cited, the abnormally high and right-sided descending aorta—*aorta descendens superior dexter*—and the low right descending aorta—*aorta descendens inferior dexter.*

Among combinations of the congenital and positional anomalies, the author mentions the high and low right position of the aorta—*arcus aortae dexter* and *aorta descendens inferior dexter.*

It is emphasized that in the radiographic examination

the study of the course of the esophagus is of great diagnostic importance.

Sixteen roentgenograms; 13 drawings; 1 table, setting forth the salient characteristics of the different anomalies.

EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

Persistent Ductus Arteriosus. Importance of Angiocardiography and Thoracic Aortography in Diagnosis and Preoperative Study. Manuel Malenchini and Teo Rock. Radiol. med. (Milan) **36:** 992–997, December 1950. (In Italian)

The authors report a case of patent ductus arteriosus in a woman 24 years of age in which the angiocardiogram obtained after injection of dye in the antecubital vein showed an aneurysmal dilatation of the left branch of the pulmonary artery. Two days later, aortography performed by means of a catheter inserted in the left carotid showed the presence of a large patent ductus with reflux of the dye into the aneurysmatic pulmonary artery. This case report, illustrated by excellent roentgenograms, indicates the diagnostic difficulties which can be encountered in the study of the heart and great vessels.

Seven roentgenograms.

CESARE GIANTURCO, M.D.
Urbana, Ill.

Right-Sided Aortic Arch. Philip Samet and Daniel J. Stone. Am. Heart J. **40:** 951–954, December 1950.

The authors give the history of a 44-year-old asthmatic male in whom a right aortic arch was discovered incidentally and demonstrated by angiocardiography. A slight displacement of the trachea to the left aroused suspicion, and a study of the esophagus showed the highly characteristic pressure indentation on the posterior wall. Neuhauser (Am. J. Roentgenol. **56:** 1, 1946. Abst. in Radiology **48:** 545, 1947) has classified right aortic arch without cardiac inversion as anterior and posterior. In the anterior type the aortic arch is in front of the trachea and the descending aorta is on the right side. In the posterior type the aorta passes to the left behind the esophagus and the descending aorta takes a course to the right of the normally placed descending aorta, but still on the left side. The posterior type is further subdivided: (1) the left subclavian artery arises last from the arch and crosses behind the esophagus; (2) no vessel arising from the arch crosses the midline posterior to the esophagus, though a vessel may pass in front of the trachea; (3) a persistent left aortic diverticulum gives origin to the left subclavian artery. The authors' case is believed to be of this last type, although the left subclavian artery was not demonstrated on the angiocardiogram.

Seven roentgenograms.

HENRY K. TAYLOR, M.D.
New York, N. Y.

Double Aortic Arch in Man. Hans Franke. Fortschr. a. d. Geb. d. Röntgenstrahlen **73:** 280–284, July 1950. (In German)

Double aortic arch is a rare congenital anomaly due to persistence of the right branchial artery. The author reports the first case of this kind in which the diagnosis was made during life.

The patient was a 69-year-old man who had suffered for the last twenty years from slight dyspnea and palpitation on exertion. The clinical examination revealed evidence of emphysematous bronchitis. The heart findings were non-contributory, except that in the right sternoclavicular area a deep pulsation was palpable. The blood pressure was normal.

The roentgenogram of the chest showed a heart of normal size and configuration, with a widening of the upper mediastinal shadow due to a right high position of the aortic arch. At the level of the third sternocostal junction, a right-angled offset was seen in the posteroanterior view caused by a lower, left-sided aortic arch of the same width. The diagnosis was confirmed by roentgenograms taken in the oblique positions. It was noted that the aorta on the right side caused an indentation and slight displacement of the esophagus, while the left aortic arch did not interfere with the normal course of the esophagus.

The radiographic examination included a visualization of the left common carotid artery and the left subclavian artery, offering further proof of the presence of a double aortic arch.

Four roentgenograms; 3 schematic drawings.

EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

Diagnosis of Tricuspid Atresia or Stenosis in Infants, Based upon a Study of 10 Cases. Benjamin M. Gasul, Egbert H. Fell, William Mavrelis, and Raul Cases. Pediatrics **6:** 862–871, December 1950.

Ten cases of tricuspid atresia or stenosis are discussed. The authors recognize two types of cases, depending upon whether or not they are amenable to surgery:

Type I: Cases of tricuspid atresia or stenosis amenable to surgery. Anatomically these patients have the following associated malformations: (*a*) an interauricular communication—either a patent foramen ovale or an interauricular septal defect; (*b*) hypoplasia or absence of the right ventricle; (*c*) hypoplasia or atresia of the pulmonary artery. In addition, they may or may not have (*d*) a patent ductus arteriosus or an (*e*) interventricular septal defect, or both.

Type II: Cases of tricuspid atresia or hypoplasia not amenable to surgery. Anatomically these patients have, in addition to the atresia or hypoplasia, the following associated malformations: (*a*) interauricular communication; (*b*) hypoplasia of the right ventricle; (*c*) complete transposition of the great vessels. The pulmonary artery, because it originates from the large left ventricle, is usually of larger caliber than the aorta, which arises from the hypoplastic right ventricle. In addition to these defects, there may be (*d*) an interventricular septal defect or (*e*) patent ductus arteriosus, or both.

Eight of the authors' cases were of Type I, and 2 of Type II. The clinical, fluoroscopic, roentgenologic, angiocardiographic, and electrocardiographic findings in both types of lesion are described.

Fourteen illustrations, including 6 roentgenograms.

The Arteria Lusoria in the Roentgenogram. A. Ravelli. Fortschr. a. d. Geb. d. Röntgenstrahlen **73:** 285–288, July 1950. (In German)

The author describes the roentgenologic characteristics of the so-called arteria lusoria, which is synonymous with the right subclavian artery. This artery originates from the aortic arch on the left side and causes a typical indentation of the esophagus.

It has previously been stated that the right subclavian artery takes a horizontal course as it passes behind the esophagus. This, however, does not hold true in all cases. Two cases were seen by the author in which the course was upward and oblique. In the first case, the vertex of the aorta was higher than normal; in the second case, the aortic arch was relatively low.

For proper radiological visualization, it is necessary to examine these cases in the oblique position with the esophagus filled with thick barium paste.

Four roentgenograms; 1 drawing.

EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

Compression of the Trachea or Esophagus by Vascular Anomalies. Surgical Therapy in 40 Cases. Robert E. Gross and Edward B. D. Neuhauser. Pediatrics **7**: 69–88, January 1951.

A description is given of five different types of anomalies of the great vessels of the superior mediastinum which can produce compression of the esophagus or trachea (or both), as observed in 40 infants and children operated upon at the Boston Children's Hospital. These malformations of the vascular system can give rise to difficulties in swallowing and to serious disturbances in pulmonary ventilation.

Double Aortic Arch: In double aortic arch the ascending aorta bifurcates into two branches, one of which passes in front of and to the left of the trachea, while the other progresses to the right and to the posterior aspect of the esophagus, both limbs then joining to form a descending aorta. Usually the anterior arch is the smaller of the two. This anomaly is generally a serious one, often leading to death within the first year or two of life because of the extreme tracheal obstruction and because of superimposed pulmonary infection.

Roentgenologic examination may reveal a pneumonitis. During inspiration the lungs may be poorly aerated, whereas during exhalation they may be hyperaerated. The trachea is narrowed in its lower portion, displaced forward, and compressed on both sides. There is a horizontal defect of the posterior wall of the esophagus at the level of the third or fourth thoracic vertebra.

Of the authors' 16 patients with double aortic arches, ranging from one month to two years of age, who came to operation, 13 had the aorta descending on the left and 3 on the right. Of the 13 with a left descending aorta, there were 9 in whom the anterior arch was the smaller of the two and was accordingly divided; in 4 the smaller posterior limb was sectioned. In the 3 patients who had double arches and a right descending aorta, it was always the posterior one which was divided. Twelve of the 16 patients were alive, greatly improved, after various intervals up to five years.

Right Aortic Arch with Left Ligamentum Arteriosum: In patients with a right aortic arch, the ligamentum arteriosum may pass to the left of the trachea and then around behind the esophagus to reach the aorta, thus completing a "ring" which compresses the trachea and esophagus. The symptoms produced by this anomaly are similar to those produced by double aortic arch but are usually less severe.

Roentgenograms of the chest may show a pneumonitis. The aortic arch is visible on the right side. During inspiration there may be incomplete aeration of the lungs, and during expiration there may be hyperaeration. The lower segment of the trachea is narrowed. There is an indentation along its right wall imposed by the aortic arch, as well as an indentation of the anterior surface of the trachea, caused by the pulmonary artery, and a depression of the left side from the ligamentum arteriosum. The esophagus has a narrow but deep constriction of its left lateral and posterior surfaces.

Seven patients with this anomaly were operated upon. In all there was striking improvement. Operation consists of division of the ligamentum arteriosum.

Anomalous Innominate Artery: The innominate artery can originate at a point farther along the arch than normal; when it does so, it must wind around the anterior surface of the trachea as it courses upward and to the right to reach the right apex of the thorax. This may cause compression of the trachea and respiratory distress.

A narrowing of the lower third of the trachea may be visible on roentgenograms. The anterior surface shows a long pronounced indentation, whereas the posterior surface appears normal.

The symptoms may be relieved by suturing the vessel to the sternum.

Four patients were operated upon and all were fully cured of their respiratory complaints.

Anomalous Left Common Carotid Artery: The left common carotid artery branches off the aortic arch more to the patient's right than is customary; it must therefore wind around the anterior surface of the trachea as it courses upward and to the left. This may compress the anterior border of the trachea and cause respiratory distress and secondary pulmonary infection.

By roentgenographic study a rather long groove is demonstrated along the anterior wall of the trachea. This may be seen to run obliquely upward and to the left.

The surgical treatment is similar to that for an anomalous innominate artery. The authors' 2 patients were completely relieved of their symptoms.

Aberrant Subclavian Artery: It is not uncommon for the right subclavian artery to take off from the distal part of the aortic arch. It ascends and must deviate to the right to reach the right apex of the chest. Rarely the artery may pass in front of the trachea; more frequently it runs between the trachea and esophagus, but in the vast majority of instances it courses behind the esophagus. This may constrict the esophagus and produce difficulties in swallowing.

Roentgenologically there is a defect of rather small caliber on the posterior wall of the esophagus at the level of the third or fourth thoracic vertebra. This indentation runs obliquely upward and toward the right.

The surgical procedure for alleviation of symptoms is the ligation and division of the vessel. Eleven patients were operated upon and all were relieved of their symptoms.

Seventeen roentgenograms; 19 drawings.

HOWARD L. STEINBACH, M.D.
University of California

Chronic Cor Pulmonale in Long-standing Bronchial Asthma. Maxwell L. Gelfand. Am. J. Med. **10**: 27–36, January 1951.

Long-standing bronchial asthma almost inevitably leads to emphysema and this, after a long period of time, results in the production of increased pulmonary tension, the forerunner of cor pulmonale. Thus the effects of bronchial asthma on the heart actually become the effects of emphysema on the heart. Recent pathological

studies have clearly demonstrated that emphysema is a frequent cause of hypertrophy and dilatation of the right ventricle.

Four cases of long-standing bronchial asthma with cor pulmonale are presented to emphasize the salient diagnostic features of this entity that may lead to its early recognition.

Cor pulmonale can and should be diagnosed clinically on the following criteria: (1) presence of long-standing bronchial asthma and emphysema without any other associated cardiac disease; (2) development of an increase in the dyspnea and cyanosis already present; (3) appearance of orthopnea with or without signs of right-sided failure; (4) the presence of increased pressure in the pulmonary circuit, either implied or directly measured by intracardiac catheterization; (5) roentgen demonstration of cardiac enlargement; (6) an electrocardiographic pattern of right ventricular hypertrophy.

Tumors of the Heart. Hans Franke. Fortschr. a. d. Geb. d. Röntgenstrahlen **73:** 299–307, July 1950. (In German)

Heart tumors are relatively rare. They are preferably classified, according to their origin, as pericardial, epicardial, myocardial, and endocardial.

The author describes 5 of his own cases. The first 3 were not treated surgically and were diagnosed roentgenologically as probable fibroma in 2 instances and possible dermoid cyst or chondroma of the heart in the third. All 3 tumors remained unchanged over an observation period of two to four years.

In the fourth case, a large round tumor in a 22-year-old male was seen in the roentgenogram on the left side of the heart, extending into the anterior mediastinum. A long cyst attached to the left atrium was surgically removed, and recovery was uneventful.

The fifth case was that of a 40-year-old female. The roentgenogram revealed a very large tumor obscuring the left chest cavity and extending over to the right side. Within this tumor twelve teeth could be seen. Because of the severe cyanosis and decompensation due to mechanical pressure, operation was done, and the diagnosis of teratoma was confirmed. The patient expired postoperatively.

The differential diagnosis and classification of tumors of the heart and of the large blood vessels are discussed in detail.

Fourteen roentgenograms.

EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

Roentgen Manifestations of Pericardial Thickening. R. Haubrich and P. Thurn. Fortschr. a. d. Geb. d. Röntgenstrahlen **73:** 288–298, July 1950. (In German)

The authors report a case of stenosis of the esophagus caused by pericardial adhesions and calcifications. The difficult differential diagnosis between internal and external adhesions of the pericardium, with or without calcification, is discussed at length. A proper diagnosis in such cases can be made only with the help of a kymographic study. In intraventricular sulcus calcifications, the tracing runs parallel to the tracing of the lateral border of the left ventricle when combined with internal adhesions and scars of the pericardium. If the latter are absent, however, the kymographic tracings run in opposite directions. This changing over from the first to the second type of movement after surgery is demonstrated and illustrated by an individual case.

In calcifications of the entire pericardial cavity, atypical kymograms are obtained and are of little diagnostic value.

Three roentgenograms; 6 kymograms; 2 drawings.

EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

THE DIGESTIVE SYSTEM

Nonspecific Granulomatous Inflammation of the Stomach and Duodenum: Its Relation to Regional Enteritis. Mandred W. Comfort, Harry M. Weber, Archie H. Baggenstoss, and William F. Kiely. Am. J. M. Sc. **220:** 616–632, December 1950.

To Crohn, Ginzburg, and Oppenheimer (J. A. M. A. **99:** 1323, 1932) belongs the credit for recognizing nonspecific granulomatous inflammation of the ileum as a clinical entity, although cases had been recorded in previous years. These authors termed the entity regional ileitis but later when it was realized that the process involved the jejunum the name regional enteritis was proposed.

In recent years it has been found that non-specific granulomatous inflammation may occur in the duodenum and the stomach as well as the jejunum, ileum, and colon, though only 2 cases with duodenal and 1 with gastric involvement were found in the literature. The authors have selected for presentation 5 cases of nonspecific granulomatous inflammation of the stomach and duodenum from a larger number seen at the Mayo Clinic, to direct attention to the fact that the disease process does affect this part of the digestive tract. The term "non-specific granulomatous gastroenteritis" thus appears to be a more suitable name than the older and less precise designations.

The five cases reported here had much in common clinically, roentgenologically, and pathologically. Clinically, four features were outstanding, continuous and intermittent upper abdominal distress, diarrhea, gastric retention, and evidence of deficient absorption. Roentgenologically, the picture was that of disturbed motility of one or more portions of the upper part of the gastro-intestinal tract with or without persistent or transitory constriction and dilatation. Histologic study of material from the walls of the pylorus and duodenum and jejunum, as well as examination of the mesenteric nodes, disclosed inflammatory process.

Ten roentgenograms; 4 photographs; 5 photomicrographs.

H. A. O'NEILL, M.D.
Cleveland, Ohio

Mesenchymal Tumors of the Stomach. Charles J. France and Osborne A. Brines. Arch. Surg. **61:** 1019–1035, December 1950.

Included in the group of mesenchymal tumors are all neoplasms arising from the various components of the gastric wall, exclusive of the surface lining, *i.e.*, tumors arising from muscle, connective tissue, fat, nerve, blood vessels, and lymphoid tissues. The following classification is proposed.

Histogenesis	*Benign*	*Malignant*
Myogenous	Leiomyoma	Leiomyosarcoma
Fibroblastic	Fibroma	Fibrosarcoma
	Myxoma	Myxosarcoma
Lipoblastic	Lipoma	Liposarcoma
Endothelial	Hemangioma	Malignant angioendothelioma
	Lymphangioma	
	Benign hemangioendothelioma	
Neurogenous	Neurofibroma	Neurofibrosarcoma
	Neurilemmoma	Malignant neurilemmoma
Lymphogenous	Benign lymphoma	Lymphoblastoma

These various types are discussed, with numerous references to the literature, after which the authors turn to their own series, representing both autopsy and surgical material encountered at the Detroit Receiving Hospital in the years 1922 to 1948.

Of a total of 359 neoplasms of the stomach, 35, or 9.8 per cent, were of mesenchymal origin; 20 of these were benign and 15 malignant. The malignant group included 12 lymphomas, which are not discussed in this paper. Details of the remaining 23 cases are presented in tabular form. These included 4 leiomyomas, 8 fibromas, 1 lipoma, 2 neurilemmomas, 5 neurofibromas, and 3 leiomyosarcomas.

Benign non-epithelial tumors should be removed to avoid or alleviate such complicatons as hemorrhage, obstruction, or malignant transformation. Local excision will suffice for small tumors, but larger lesions, or multiple lesions, may require resection of a greater portion of the stomach. The prognosis following complete removal should be excellent. The five-year survival rate following resection of *malignant* mesenchymal tumors of the stomach may be expected to be 25 to 30 per cent.

Two roentgenograms; 2 photomicrographs; 5 tables.

MORTIMER R. CAMIEL, M.D.
Brooklyn, N. Y.

Incidence of Malignancy in Gastric Ulcers Believed Preoperatively to Be Benign. Elmer Graham Lampert, John M. Waugh, and Malcolm B. Dockerty. Surg., Gynec. & Obst. **91**: 673–679, December 1950.

The authors studied 73 cases of gastric cancer, in none of which was the malignant nature of the lesion determined preoperatively, either clinically or radiographically. These constituted 13 per cent of 550 cases operated upon at the Mayo Clinic with a preoperative diagnosis of benign ulcer of the stomach over a five-year period.

The average duration of symptoms was thirty-eight months, but 21 patients (28.7 per cent) gave a history of ulcer symptoms from five to forty years. In 47 patients (64.3 per cent) the symptoms were of progressive severity; in 17 (23.2 per cent) they remained unchanged; and 9 patients (12.3 per cent) experienced relief from their complaints at intervals.

The most frequent symptoms were pain of constant character, hematemesis, melena, emesis, and loss of weight. Gastric analysis was done in 66 cases, showing a normal concentration of free hydrochloric acid in 65 per cent; in 34 per cent the figure was below normal, including 21 per cent in which no free acid was present.

The authors stress the responsibility of the roentgenologist in detecting the presence of the lesion, locating it, and describing its characteristics in relation to the gastric mucosa and walls. Diagnosis of a benign ulcer implies only that no evidence of malignancy was seen; it cannot positively be ruled out.

In 21.9 per cent of this series there was an associated duodenal ulcer, and in the majority of these cases there was a long history. In many there had been a definite change in the character of the symptoms, presumably due to the neoplastic development.

Each of the 73 cases was studied pathologically; 63.8 per cent showed serosal extension or lymph node involvement. None of the ulcers was on the greater curvature.

JACK EDEIKEN, M.D.
University of Pennsylvania

Perforated Gastric Ulcer in a Newborn Infant. Lydia T. Wright and Beatrice E. Scott. J. Pediat. **37**: 905–908, December 1950.

A case of perforated gastric ulcer in a newborn infant, delivered of a pre-eclamptic syphilitic mother, is reported. It is unusual in that the typical symptoms were not present. A flat and upright film of the abdomen revealed a massive pneumoperitoneum, with high position of the diaphragm and displacement of the abdominal viscera. The infant died before operation could be performed.

One roentgenogram; 1 photomicrograph.

Thoracic Stomach Simulating Left Ventricular Failure. Henry H. Haft and Daniel K. Adler. Ann. Int. Med. **33**: 1472–1479, December 1950.

The authors report a rather unusual case of diaphragmatic hernia in which the entire stomach was shown roentgenographically to lie within the posterior mediastinum. The patient had suffered from "stomach trouble" for many years and more recently had experienced sudden attacks of severe dyspnea which had been attributed to cardiovascular disease until roentgen study revealed the true state of affairs. The heart contour was normal on examination and an electrocardiogram showed no evidence of myocardial damage.

Three roentgenograms.

Gastric Residue in Cholecystography. Charles Gottlieb and Samuel L. Beranbaum. Am. J. Digest. Dis. **17**: 389–394, December 1950.

A series of 7 cases is presented to show that gastric residue when seen at cholecystography should never be ignored but should always be followed by examination of the stomach. In 5 of the 7 cases it proved to be indicative of a lesion in the stomach or duodenum.

Case 1 showed a normal functioning gallbladder but there was a small fleck of dye in the region of the bulb. X-ray examination of the stomach showed a duodenal ulcer.

In Case 2, two attempts at visualization of the gallbladder failed, but dye remained in the stomach. Gastro-intestinal examination showed a large duodenal ulcer producing marked obstruction.

In Case 3, the gallbladder was visualized but a gastric residue of priodax was observed on the cholecystograms. A gastro-intestinal series was done and a large gastric ulcer was found and subsequently resected.

In Case 4, cholecystography was done in an attempt to determine whether disease of the gallbladder might account for attacks of severe precordial pain, which could not be explained otherwise. No gastro-intestinal symptoms were present, but operation revealed a "large nodular mass involving most of the body of the stomach," as well as a metastatic nodule on the under surface of the liver.

Case 5 showed a non-functioning gallbladder with a small amount of radiopaque residue in the stomach. The finding of the residue was disregarded and the patient came to surgery. A large perforated ulcer was found in the second portion of the duodenum, involving the head of the pancreas.

In the remaining cases cholecystograms showed non-visualization of the gallbladder and gastric retention of priodax. In one gallstones were found at operation; in neither was there any gastro-intestinal disease.

In their conclusions, the authors point out that gastric residue during cholecystography represents a

residue of at least fourteen hours duration and, as such, is highly significant as an index of altered motility. Therefore, the likelihood of finding a gastric or duodenal lesion (not necessarily obstructive) is much greater than in those cases with six-hour gastric residue during the usual gastro-intestinal series with barium sulfate. It is also pointed out that non-visualization of the gallbladder is not synonymous with disease of that organ, especially in the presence of delayed gastric evacuation of priodax, which is insoluble in the acid gastric juice.

Ten roentgenograms. JOSEPH T. DANZER, M.D.
Oil City, Penna.

Diagnosis of Early Intestinal Cancer. Harry M. Weber. Am. J. Roentgenol. **64**: 929–937, December 1950.

In the eighth annual Carman lecture given under the auspices of the St. Louis County Medical Society, the author describes fully the role of the radiologist and proctosigmoidoscopic examiner in detecting early cancer of the colon.

Rectal and sigmoid lesions can and should be discovered at the proctoscopic examination if the lesion is at least 0.5 cm. in diameter and is within reach of the usual 25-cm. sigmoidoscope. Roentgenologic examination can never be as effective in these areas and it should not be used as a substitute for good direct visualization. Lesions of the remainder of the colon, the author believes, can be detected by roentgenologic examination at least as early in their development as they will manifest themselves by clinical signs and symptoms. For practical purposes the lower limit of size of lesions demonstrable roentgenologically is probably about 1 cm. (diameter). It is believed that the roentgen examination of the large intestine can be made to elicit reliable evidence of small polypoid lesions without having a significant number of them escape detection.

The appearance of early intestinal cancer is usually polypoid, though all small polypoid lesions are certainly not malignant.

Mass surveys for the discovery of early colon cancer are impracticable, but the author considers it imperative to submit to thorough intestinal investigation any patient who has one or more of the following clinical signs and symptoms: (1) chronic loss of blood, manifested most frequently by melena and less frequently by anemia; (2) significant and persistent alteration in the functional activity of the intestine; (3) abdominal pain of colicky, crampy type; (4) abdominal tumor.

Ten illustrations, including 7 roentgenograms; 2 tables. RICHARD A. ELMER, M.D.
Emory Medical School

Distribution of Gas in the Intestine Following Laparotomies Unaccompanied by Complications. Nils Liedberg and Stig Berglund. Acta radiol. **34**: 493–500, December 1950.

A daily survey of the abdomen in supine and lateral decubitus positions was performed on 50 patients who underwent laparotomy with an uneventful postoperative course. Accumulation of gas was found to be less marked and more rarely demonstrable after brief operative procedures such as simple appendectomy. More lengthy operations, such as those on the biliary tree and stomach, gave rise to large accumulations of gas in the small intestine, which were most pronounced during the second day and had usually gone after four days. No fluid levels were observed in any of the cases. The presence of fluid levels is thought to presage the advent of a disturbance in intestinal patency.

Nine roentgenograms. JOHN F. RIESSER, M.D.
The Henry Ford Hospital

Cholecystitis and Cholelithiasis in Young Women Following Pregnancy. Walter H. Gerwig, Jr., and J. Richard Thistlethwaite. Surgery **28**: 983–996, December 1950.

The authors report 10 cases of cholecystitis and cholelithiasis in women under thirty years of age, for which operation was done in a six-month period. In all these cases, symptoms began either during or shortly after pregnancy. The chief complaints were pain, intolerance to fatty foods, and other generally accepted symptoms of biliary tract disease. Six patients had severe colic. Examination with priodax showed a non-functioning gallbladder in 7 instances. At operation, 5 patients were found to have obstruction of the cystic duct. All had calculi and varying degrees of change in the gallbladder wall indicative of cholecystitis.

The authors point out that hypercholesterolemia occurs in association with pregnancy, lactation, the menopause, convalescence from typhoid fever, diabetes, obesity, hypothyroidism, and arteriosclerosis, and that the incidence of gallstones in all these conditions is high. In pregnancy, the blood level for cholesterol may be increased 300 to 400 per cent and, since cholesterol is excreted by the liver cells into the bile and is concentrated by the action of the gallbladder mucosa, excessive amounts in the gallbladder may crystallize and produce stones.

In order to prevent acute cholecystitis, perforation of the gallbladder—which occurs in about 10 per cent of such cases—longstanding inflammation, cholangitis, and hepatic damage, the authors advocate early surgery in young parous women with evidence of gallbladder disease.

In addition to tables analyzing the findings in the patients studied, there are 6 figures illustrating the roentgen observations as well as the gross and microscopic appearance of the involved gallbladders.

WILLIAM H. SMITH, M.D.
University of Louisville

Dysfunctioning, Non-Calculous Gallbladder. James F. Crenshaw. Am. J. Digest. Dis. **17**: 387–389, December 1950.

An attempt has been made by the author to evaluate the significance of the gallbladder that, although filling normally, fails to empty well after a fatty meal. There is no definite criterion by which to measure the amount of emptying which should take place in a given period, but it is believed that a normally functioning organ should empty half its contents in three hours. As a rule, it is half empty thirty minutes after a fatty meal.

The gallbladder under normal conditions fills when the sphincter of Oddi is closed and empties when it is open. With contraction of the gallbladder, relaxation of the neck and the cystic and common ducts takes place and the sphincter of Oddi opens, allowing free ingress of bile into the duodenum. A powerful stimulant to gallbladder contraction is the hormone cholecystokinin, which is secreted by the mucosa of the duodenum and upper jejunum under the stimulus of fat.

Derangements of any of the normal evacuating mechanisms may lead to delayed emptying of the gallbladder. Abnormally thick mucus or bile will produce stagnation. Deficiencies of cholecystokinin also have a significant effect on the emptying power. Among other intrinsic causes of dysfunction are damage to the gallbladder wall, kinking of the neck, spasm of the cystic duct, dysfunction of the reciprocal mechanism of gallbladder and sphincter of Oddi, reflex and nerve abnormalities. Chief among the extrinsic causes are disturbances within the gastro-intestinal tract, such as hypochlorhydria, pyloric spasm or obstruction, peptic ulcer and ileus. Pregnancy, hypothyroidism, allergy, and drugs of the morphine group, which cause a spasm of the sphincter of Oddi, have been shown to interfere with evacuation.

In a study of 500 consecutive cholecystograms, the author found 107 cases of sluggish emptying of the gallbladder. Typical gallbladder complaints were registered by 38 of these patents, while 69 had atypical digestive symptoms. Only 12 had typical acute gallbladder attacks. In studies made to find the cause for the sluggish emptying, no clear-cut explanation could be found. Only 9 persons were as much as 15 pounds overweight. Basal metabolism tests, done in 54 patients, were within the normal range in 23, while 4 showed hypermetabolism and 27 hypometabolism. Gastric analyses showed definite hypochlorhydria in 25 of 69 patients. X-ray studies of the gastro-intestinal tract, done in 93 cases, revealed some hypertonicity in 67; 4 patients were found to have a duodenal ulcer.

The control of gallbladder disease is governed by three factors: (1) the etiological basis, as infection, stasis, and metabolic abnormalities, (2) cholecystographic findings, and (3) evaluation of clinical manifestations. A medical regime based on an attempt to stimulate a more normal flow of bile should be attempted. Non-surgical gallbladder drainage, bile salt therapy, and attention to diet are recommended.

JOSEPH T. DANZER, M.D.
Oil City, Penna.

Annular Pancreas. Mark M. Ravitch and Alan C. Woods, Jr. Ann. Surg. **132:** 1116–1127, December 1950.

Annular pancreas is a rare congenital anomaly which may or may not produce obstruction of the duodenum. In only 17 cases, including 3 reported in detail here, has operation been done for relief of symptoms. Many cases have been incidental necropsy findings. The diagnosis may be made in patients with chronic duodenal obstruction who show by roentgen ray an almost complete, smooth and sharp obstruction of the duodenum to the right of the midline. Barium meal studies are frequently not conclusive.

Two of the authors' patients were infants, three and eight days of age, with findings typical of neonatal duodenal obstruction from whatever cause. In the third patient, a man of sixty-seven years, the diagnosis was made roentgenographically.

Duodenojejunostomy is regarded as preferable to resection because of the leakage of pancreatic enzymes if the encircling pancreatic tissue is divided. Fistulae and pancreatitis or peritonitis have occurred in the majority of cases where resection was tried.

Ten roentgenograms; 1 drawing.

[A case of annular pancreas in a three-and-a-half-year-old boy, diagnosed tentatively from the roentgenogram and successfully operated upon, is reported by Haden in a recent issue of Radiology (**55:** 859–860, 1950).—Ed.]

ZAC F. ENDRESS, M.D.
Pontiac, Mich.

Mesenteric Cysts—A Case Report. E. M. Crawford, J. J. Griffith, and P. H. Roberts. J. Canad. Assoc. Radiologists **1:** 75–76, December 1950.

Cysts of the mesentery are rather rare and the diagnosis can be made only after opacifying the gastro-intestinal and genito-urinary tracts and proving them to have no connection with a palpable, movable, non-tender mass, usually visible on a plain film of the abdomen. Most contain a watery fluid; calcification is rare. The origin is usually embryonic, with a number of possibilities as listed in the classification given by Peterson (Ann. Surg. **112:** 80, 1940). An inflammatory or neoplastic origin is also possible.

In the case reported here a gastro-intestinal study showed displacement of the duodenal loop to the left and of the proximal transverse colon downward. At laparotomy a cyst "about the size of a grapefruit" was found in the peritoneal folds, along with a second smaller one.

Two roentgenograms. ZAC F. ENDRESS, M.D.
Pontiac, Mich.

THE MUSCULOSKELETAL SYSTEM

Age Determination. Conflicting Evidence Presented by Anatomical and Radiological Data of the Skeleton. J. A. Keen. South African M. J. **24:** 1086–1089, Dec. 30, 1950.

This discussion of the anatomical and radiological methods of age determination appears to have been prompted by a legal case in which radiological demonstration of epiphyseal fusion was offered— unjustifiably—as evidence that the defendant was more than sixteen years of age. It is pointed out that radiological evidence cannot be interpreted on the basis of age data collected by anatomists; neither can anatomical evidence of union or non-union of epiphyses be interpreted with the help of age data compiled by radiologists, because the criteria indicating epiphyseal fusion will be shown to be different in the two methods.

Actually "radiological fusion" precedes the disappearance of visible epiphyseal lines in anatomical specimens. Epiphyseal lines may remain visible at the extremities of long bones long after evidence of non-union has disappeared on the roentgenogram. The various anatomical changes which occur toward the end of the growth period make it more and more difficult for radiography to reveal the existence of an epiphyseal plate of cartilage as a break in the continuity of the bone. The line of the break not only becomes thinner, but its shape becomes irregular, so that continuity in the bony pattern at one level overlaps, and may obscure or even hide, a break in continuity at another level. Allowance must also be made for superimposition of the soft parts, which tends to obscure the display of epiphyseal lines.

It is concluded that in our present state of knowledge, the anatomical and radiographic criteria for age determination cannot be reconciled, and must be treated as separate entities. If in a particular case radiological evidence alone is available, a deduction of "probable age" must be made on data supplied by radiologists. Vice versa, if the actual bones can be inspected, the

periods of epiphyseal fusion established by anatomists can be used in order to make a deduction of "probable age."

Five roentgenograms; 4 paired photographs and roentgenograms. S. F THOMAS, M.D.
Palo Alto, Calif.

A Case of Melorheostosis. Marja Koulumies. Acta radiol. **34**: 529–532, December 1950.

The first case of melorheostosis, or Léri's disease, known in Finland is presented. Involvement was confined to the right upper extremity. At the age of twenty-three, the patient noticed a protuberance at the right elbow with some associated pain. Roentgen examination at that time showed compact tuberous osteal hypertrophy in the right radius and wrist. No other bones were examined and no diagnosis was made. The pain in the elbow was relieved by roentgen therapy. Nine years later pain recurred and renewed growth was noted in the old osteal protuberance. More adequate study at this time revealed osteosclerotic, structureless, thickened bone in the right upper extremity showing the flowing, candlegrease outline typical of melorheostosis. An attempt is made to relate the changes to insignificant trauma at an early age, but this does not appear warranted.

Four roentgenograms. JOHN F. RIESSER, M.D.
The Henry Ford Hospital

Progressive Diaphyseal Dysplasia (Engelmann's Disease). James B. Gillespie and Robert D. Mussey. J. Pediat. **38**: 55–59, January 1951.

A case of progressive diaphyseal dysplasia (Englemann's disease) is presented. The patient was first seen in November 1948 at the age of thirty-three months, and is the youngest of the 8 patients reported to date. The syndrome is characterized by progressive symmetrical enlargement and cortical thickening in the diaphyses of the long bones. The clinical findings include muscular weakness with a waddling gait, failure to gain weight properly and, occasionally, neurologic variations.

Roentgen studies in the authors' case demonstrated lesions in all long bones, the skull, and the clavicles. It was thought that some involvement of the ribs was also present, although of insufficient degree to be conclusive. From June 1949 to July 1950 no significant changes occurred in the femurs, but a slight progressive involvement of the tibias and fibulas was evident.

Four roentgenograms.

Osteoporosis and Diffuse Plasmocytosis. E. Morvay. Fortschr. a. d. Geb. d. Röntgenstrahlen **73**: 349–357, July 1950. (In German)

The author describes a case of diffuse plasmocytosis in a 42-year-old patient with a history of spontaneous fractures of many bones over a period of years, though the general health was good. The case was under observation for three and a half years. A generalized diffuse osteoporosis was present. A severe anemia developed two months before death.

It is emphasized that diffuse plasmocytosis is not a disease in itself but represents a stage of multiple plasmocytoma. Diffuse plasmocytosis leads to severe generalized bone atrophy with cyst-like lesions in the flat bones, especially the skull and scapula. The appearance of the bones is similar to that in ordinary osteoporosis. Bone metastases are the first consideration in differential diagnosis.

Seven roentgenograms; 1 drawing; 1 photomicrograph. EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

Reticulum Cell Sarcoma of the Rib. Herbert R. Corbett. J. Canad. Assoc. Radiologists **1**: 69–71, December 1950.

Reticulum-cell sarcoma of the bone is a relatively rare tumor. The majority of the reported cases have been in the long bones, but the flat bones may be involved as well. Osteolysis is the rule, usually with some reactive new bone formation. Growth is said to be rapid, with metastasis to the lungs and lymph nodes. It is of interest that patients may remain in comparatively good health even after the disease is advanced.

The author's patient was first seen as an out-patient three years before admission. On that occasion a tumor of the second rib was disclosed on x-ray examination. Biopsy was recommended but was not done, and the patient was lost sight of until he returned (in 1950) with metastases in the skull, eleventh rib, and left inguinal region. Biopsy of the metastatic rib lesion revealed a reticulum-cell sarcoma. X-ray therapy was advised but refused. Death occurred nine months after the diagnosis was made.

Two photomicrographs. ZAC F. ENDRESS, M.D.
Pontiac, Mich.

Multiple Fractures Associated with Subdural Hematoma in Infancy. Edward F. Lis and George S. Frauenberger. Pediatrics **6**: 890–892, December 1950.

The association of multiple long bone fractures with subdural hematoma in 6 infants was reported by Caffey in 1946 (Am. J. Roentgenol. **56**: 163, 1946. Abst. in Radiology **48**: 657, 1947). A case similar to those described by Caffey, differing only in that the fractures predominated in the flat rather than the long bones, is reported.

The factors responsible for the coincidence of multiple fractures with subdural hematoma in infancy are obscure. Caffey suggested a traumatic origin, but a history of injury was lacking in the patients in his series and in the authors' case. Nor has there been any evidence of local or systemic skeletal disease.

Two roentgenograms.

Distention-Dislocation in the Roentgenogram. Fritz Klopfer. Fortschr. a. d. Geb. d. Röntgenstrahlen **73**: 357–361, July 1950. (In German)

The author calls attention to the fact that interarticular inflammatory processes in the region of the hip joint may cause such pressure within the joint capsule that a dislocation of the femoral head can occur without bone destruction. He describes the case of a child of fifteen months in whom a tuberculous exudate was responsible for a dislocation of the hip. There were no bony changes present.

In a second child, one year of age, a subluxation of the right hip, apparently due to a traumatic exudate, was observed. After fixation of the joint and absorption of the exudate, the position of the femoral head returned to normal.

Seven roentgenograms.
EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

Synovial Sarcoma (Malignant Synovioma). George T. Pack and Irving M. Ariel. Surgery **28**: 1047–1084, December 1950.

Synovial sarcomas as considered here are those malignant neoplasms which arise from synovial tissue—of joints, tendon sheaths, and bursae—and which present histologic features characteristic of synovial tissue. They have also been designated as "synovioma" and for that reason this latter term should never be employed to designate a benign lesion.

The authors analyze and present the pathologic and clinical features of 60 cases of synovial sarcoma observed from 1931 to 1948 inclusive, and constituting 8.4 per cent of all malignant neoplasms of the soft somatic tissues studied on the Mixed Tumor Service of the Memorial Hospital, New York.

The disease is essentially one of younger adults. Sixty per cent of the tumors in this series occurred between the ages of fifteen and forty years. The sexes were equally affected.

No etiologic factor was established in the series, although in several cases trauma preceded the symptoms and in 3 patients the possibility of benign tumor of synovia undergoing malignant change was suggested.

The tumors were usually extra-articular, the most frequent location being the popliteal space. No characteristic symptom complex or roentgenographic features were observed. The diagnosis must be established by biopsy. The usual roentgen finding was a soft-tissue density, usually in the vicinity of a joint. Calcification was present occasionally. The adjacent bone was normal or distorted by pressure or invasion by the primary tumor or its metastases. When invasion occurred, the lesion was destructive. Metastases were of the osteolytic type.

A recurrence rate of 63.3 per cent was observed, and in 26.6 per cent of the patients a second recurrence developed.

The absolute five-year survival rate was 19.1 per cent. The relative five-year survival rate was 20.5 per cent, and the therapeutic five-year survival rate was 23.5 per cent. The authors state that radical surgery is the one suitable method of ablating synovial sarcoma and that radiation therapy may be used to supplement surgery or for palliation. It is interesting to note that in the present series the best results were obtained with surgery plus postoperative irradiation.

Ten patients were treated with surgery alone, and of these none were alive at the end of five years. Fourteen patients were treated with surgical resection and postoperative irradiation, and of these 4 were alive after five years.

Nine illustrations; 9 tables.

WILLIAM H. SMITH, M.D.
University of Louisville

A New Familial Case of Cutis Gyrata with Pachyperiostosis of the Extremities, Verified Anatomically. A. Franceschetti, R. Gilbert, D. Klein and P. Wettstein. Schweiz. med. Wchnschr. **80**: 1301–1306, Dec. 9, 1950. (In French)

Among about 50 cases of cutis gyrata with associated bone changes reported thus far, this is the ninth in which a definite familial factor is noted. An uncle of the 43-year-old male patient presented here had the same condition. Pathologic changes include a thickening of the adnexal structures of the skin, including sebaceous glands and connective tissue. Thickening of the eyelids is present. There is an associated cortical hyperostosis of long, short, and flat bones, symmetrically distributed. There is no line of demarcation, such as is seen in hypertrophic pulmonary osteoarthropathy, and the primary etiologic factor of the latter is missing. It is concluded that the condition should be classified among systemic affections of mesenchymatous tissues.

Four roentgenograms; 4 photographs.

CHARLES NICE, M.D.
University of Minnesota

OBSTETRICS AND GYNECOLOGY

Volumetric Capacity of the Human Nulliparous Uterus. Abner I. Weisman. Am. J. Obst. & Gynec. **61**: 202–204, January 1951.

Weisman has determined the amount of iodochloral necessary to fill the uterine cavities, before filling of the tubes, in 800 previously infertile and nulligravid women. No cases of bilateral tubal closure are included in the report, since this condition would tend to produce distention of the uterine cavity with oil. Uterine cavities showing evidence of intra-uterine fibroids and polyps were also omitted from the study.

The author divides his results into three categories: (1) atrophic uterine cavities (holding 1.0 c.c. or less), (2) normal (holding between 1.0 and 2.2 c.c.), (3) hypertrophic (holding more than 2.2 c.c.). There were 27 atrophic cases, 739 normal cases, and 34 hypertrophic cases.

The conclusion drawn is that 3 to 4 c.c. of iodized oil are usually sufficient for routine hysterosalpingography. Injection of larger amounts is both unnecessary and inadvisable.

T. FREDERICK WEILAND, M.D.
Jefferson Medical College

Traumatic Intra-Uterine Adhesions. Joseph G. Asherman. J. Obst. & Gynaec. Brit. Emp. **57**: 892–896, December 1950.

As a sequel to curettage, conglutination of portions of the opposing walls of the uterine muscularis may occur, with regional obliteration of the uterine cavity. Except for sterility or habitual abortion, clinical symptoms are absent, and the diagnosis can be made only by roentgenography. Every case of habitual abortion, or sterility following abortion, should be examined roentgenologically.

The hysterograms show defects in the uterus which may be described as window-like, heart-shaped, tree-like, round, or long, or sometimes of indefinable bizarre shape. Confusion with polyps, submucous fibroids, or air bubbles should be easily avoided.

The treatment is surgical, and consists in separating the adhesions.

Eight case histories are included, with 15 roentgenograms.

MORTIMER R. CAMIEL, M.D.
Brooklyn, N. Y.

THE GENITO-URINARY SYSTEM

Excretory Urography—A Clinical Study. George H. Ewell and Harold W. Bruskewitz. Urol. & Cutan. Rev. **54**: 714–717, December 1950.

Feeling a need for improvement in the quality of excretory pyelography, the authors analyzed the effects of various combinations of preparatory procedures: alkalinization, use of pitressin, nembutal, and papav-

erine. Diodrast was the contrast medium in most cases, with neo-iopax in a few.

With diodrast, the best results were obtained with a combination of nembutal, pitressin, and alkalinization (2 ounces of citrocarbonate for the average adult), but the results were almost as good with other combinations which included pitressin or alkalinization. Papaverine and nembutal alone gave the lowest percentage of good films.

With neo-iopax the percentage of diagnostic films was lower than with diodrast and any of the preparatory measures mentioned, and the results were not improved by pitressin and alkalinization. No compression was used in either series, and no cathartics or enemas.

Since in any lesion which causes stasis the urogram is practically always satisfactory [provided there is function remaining], the authors believe that some method of producing temporary stasis should be developed.

ZAC F. ENDRESS, M.D.
Pontiac, Mich.

Retrocaval Ureter: A Case Report. S. A. Sabatini and Gerald Wessler. Urol. & Cutan. Rev. **54**: 720–721, December 1950.

Retrocaval ureter is due to an anomaly in the development of the inferior vena cava. The diagnosis is made by retrograde pyelography, which shows a sickle-shaped or S-shaped deformity of the upper third of the ureter, with the middle third displaced medially over the vertebral bodies of the lower lumbar spine.

In spite of the characteristic picture, the authors' case (the 41st in the literature) is believed to be only the sixth in which a preoperative diagnosis has been made. The patient was sixty-three years old, and nephrectomy was done because of advanced disease in the kidney. In younger patients with fair to good renal function, attempts should be made not only to conserve the kidney, but also to obviate surgical ureteral strictures.

Anyone who has not seen an illustration or an actual case of this anomaly is referred to this article. Once seen, the anomalous course of the ureter will thereafter be recognized at a glance.

One roentgenogram. ZAC F. ENDRESS, M.D.
Pontiac, Mich.

Ureteral Obstruction in Carcinoma of the Cervix. C. W. Aldridge and J. T. Mason. Am. J. Obst. & Gynec. **60**: 1272–1280, December 1950.

Ureteral obstruction in association with carcinoma of the cervix may be due to any of several causes: (1) compression or infiltration of the ureter by carcinoma; (2) irradiation changes—edema during treatment or fibrosis and scarring at a later date; (3) infection.

The authors' study is based on 333 cases of cervical carcinoma seen in the University of Michigan Hospital in which pyelographic studies were done. Of these, 34 per cent showed evidence of ureteral obstruction. This figure parallels closely the incidence of uremia as a cause of death (40 per cent) in an autopsy series from the same institution (De Alvarez: Am. J. Obst. & Gynec. **54**: 91, 1947). Treatment by dilatation or nephrostomy did not appear to improve the prognosis.

In the cases examined microscopically, the authors found the ureter to be surrounded by neoplasm, and they believe this to be the principal cause of obstruction rather than fibrosis or scarring incident to irradiation. They observed regression of hydronephrosis with decrease in demonstrable pelvic neoplastic involvement after roentgen therapy in one case. Furthermore, whenever ureteral obstruction developed, there was associated clinical advancement of the neoplasm. It was also noted that ureteral obstruction commonly occurs on the side of the greatest palpable pelvic involvement.

Six roentgenograms; 2 photomicrographs; 3 tables.

JOHN M. KOHL, M.D.
Jefferson Medical College

Müllerian Duct Cysts. Frederick A. Lloyd and Dovell Bonnett. J. Urol. **64**: 777–782, December 1950.

Retroprostatic cysts in the midline usually arise from rests of the müllerian duct. The normal remnants of the müllerian duct in the adult male are the appendix testis proximally and the prostatic utricle distally. The intervening portion of the duct, if it persists into adult life, will travel up the spermatic cord and through the inguinal ring, to join on the posterior surface of the bladder the duct from the opposite side. The ducts are intimately connected with the bladder musculature, the prostate, and the seminal vesicles.

Cysts may arise along any portion of a persistent müllerian duct. These cysts may be small and unilocular or huge and multilocular, containing as much as 5 liters of fluid. In the prostate they tend to be more firm and solid.

Most of the patients are in the third decade of life but cases have been seen in the newborn. Impotence, pain on ejaculation, difficulty in voiding, and retention of urine are common complaints. Larger cysts may compress the rectum and bladder. Small cysts may not be found on rectal examination but larger ones are palpable as a recto-vesical, fluctuant, globular mass in the midline; they may simulate a soft, symmetrically enlarged prostate or an over-distended bladder.

If the utricle can be catheterized, the cyst may be injected with radiopaque material and the diagnosis confirmed. This has been done in 3 reported cases, and should be attempted whenever the condition is suspected.

Surgical excision of the cysts is difficult due to their intimate adherence to the seminal vesicles or fusion with the bladder or prostate. Mere drainage, with partial removal and electrocoagulation, is attended by varying success.

A case is reported in a 26-year-old Negro with bilateral epididymitis, dysuria, difficulty in starting the urinary stream, and frequency. The prostate was greatly enlarged and was seen to bulge deeply into the bladder on cystoscopic examination. Sarcoma was suspected, but upon catheterization of the utricle and injection of 60 c.c. of skiodan, the cyst was clearly outlined. Surgical excision of the mass from a perineal approach, necessitating resection of part of the prostate and seminal vesicles and posterior wall of the bladder, was accomplished with difficulty and the patient made a good recovery.

Two roentgenograms; 1 photograph.

ROBERT P. BOUDREAU, M.D.
University of Pennsylvania

Roentgenological Visualization of the Genital Tract in Pseudohermaphrodism. Robert J. McCaffery. J. Urol. **64**: 701–708, December 1950.

Absolute diagnosis of the true sex in pseudohermaph-

rodism in children is difficult and places a great burden upon the physician who attempts to correct genital abnormalities. The removal of the clitoris, while a simple procedure, should be confined to those patients with well developed tubes, uterus, and upper vagina. These structures can be outlined roentgenographically with lipiodol. This should be done in all instances of genital abnormality before surgery is contemplated. This x-ray procedure differs from the usual type of hysterosalpingography only in that stress is laid upon the visualization of the vagina as to its size, development, and outer opening. In pseudohermaphrodites the vagina frequently opens into the urethra or urinary bladder. If no external vaginal opening is seen, lipiodol should be injected into the urethra.

Four cases are reported.

Ten illustrations, including 5 roentgenograms.

RICHARD V. WILSON, M.D.
University of Pennsylvania

THE BLOOD VESSELS

Aneurysms of the Splenic Artery. Thomas H. Palmer. New England J. Med. **243:** 989–993, Dec. 21, 1950.

The splenic artery is a rare site for formation of an aneurysm but it is important to be able to recognize the condition. Before rupture, surgical removal or at least ligation of the artery should not be hazardous, but in ruptured cases the mortality is high.

There are three major causes of aneurysm of the splenic artery. Arteriosclerotic aneurysms are the most common and are characterized by atheroma formation and calcification in the aneurysm wall. They usually arise along the course of the main artery. Mycotic aneurysms are produced by embolism from vegetations on the heart valves and are usually found in the branches of the artery. In some cases the aneurysm develops from a congenital defect in the wall of the splenic artery, usually at a point of branching. Four cases have been reported subsequent to trauma, but in only one was there definite evidence of the causal relation of preceding trauma. A few cases have been associated with Banti's disease or with syphilis.

Clinically there may be no symptoms or pain; vomiting and melena may occur. Physical examination reveals a mass in the left upper quadrant, usually with expansile pulsation. A bruit may be heard over the mass. Calcification in the wall of the aneurysm has usually been the factor leading to a roentgenologic diagnosis. The calcific deposits form a round or oval shadow of increased density in the upper segment of the left side of the abdomen. The periphery is delineated by a thin line of calcification, which may be interrupted in one or more places, creating a "cracked eggshell" appearance. The central portion is faintly mottled. The exact position may be determined by gastrointestinal barium studies and excretory or retrograde urography. By these methods the lesion is found to occupy a position posterior or posteromedial to the middle portion of the stomach, above the splenic flexure of the colon and superior to the upper pole of the left kidney. The center of the aneurysm is usually at the level of the twelfth thoracic or first lumbar vertebra. The roentgenographic picture may be similar to that of pancreatic cysts; however, in the latter calcification is rare.

The author reports a case in which calcification was not present. A plain film demonstrated a soft-tissue mass in the left hypochondriac region and further studies showed displacement of the left kidney downward and of the stomach anteriorly. A cyst of the spleen was suspected and operation was undertaken. The aneurysm was successfully excised. It is interesting that in this case the spleen was left in place, its blood supply being maintained by the short gastric arteries.

Two roentgenograms; 1 photograph.

ZAC F. ENDRESS, M.D.
Pontiac, Mich.

MISCELLANEOUS

Roentgenological Aspect of Infectious Mononucleosis. Julian Arendt. Am. J. Roentgenol. **64:** 950–958, December 1950.

The diagnosis of infectious mononucleosis can be definitely established only on the basis of (1) a hematological picture showing the presence of the "atypical" lymphocytes and the high percentage of such lymphocytes, and (2) the heterophile antibody test, complemented by the "differential" test developed by Davidsohn (J. A. M. A. **108:** 289, 1937). This latter test, when positive, specifically indicates the presence of infectious mononucleosis. Yet no test is positive in each case and the tests are frequently negative during the first week or two weeks of the infection. It is particularly during this period that roentgen examinations may be of value.

The roentgenologic findings in infectious mononucleosis consist first in visibly enlarged hilar lymph nodes, sometimes in the absence of external adenopathy. In no case observed by the author has this hilar lymph node enlargement produced masses large enough to be suggestive of lymphoblastoma. Fine linear strands may be seen radiating from the hili, in some cases surrounded by spotty densities and intense enough to be interpreted as pneumonia. A third roentgenological feature is splenic enlargement.

The frequency of hepatitis with or without jaundice in infectious mononucleosis may lead to roentgen examination of the stomach, which will reveal a hypertrophic gastritis. Gallbladder studies may result in non-visualization. Examination of the colon is particularly contraindicated. Mesenteric lymph nodes may give direct and indirect signs of enlargement and thus contribute to a diagnosis.

Eight roentgenograms.

RICHARD A. ELMER, M.D.
Emory Medical School

Visualization of the Abdominal Aorta and Its Branches Following Intravenous Injection of Contrast Medium. A Report of Four Cases. Ted F. Leigh and James V. Rogers, Jr. Am. J. Roentgenol. **64:** 945–949, December 1950.

The authors describe their method of visualization of the abdominal aorta using 50 c.c. of 70 per cent diodrast. The injection of the medium is made according to the Robb-Steinberg technic. An initial 14 × 17-inch Bucky film is exposed at the estimated instant of abdominal aortic filling. The interval is determined by the patient's circulation time and is usually about 10 seconds from the end of the injection. Three subsequent films are exposed at short intervals (four seconds or less). Satisfactory visualization of the abdominal aorta, its major branches, and the opacified renal paren-

chyma was obtained in a small group of patients. Four case reports are presented, 2 with illustrative roentgenograms. In one case the left renal artery was apparently obstructed by a thrombus. Two cases of obstruction in the abdominal aorta were seen, in one of which autopsy showed a thrombus obliterating the left renal artery. In another case a clinically suspected abdominal aortic aneurysm was disproved by visualization of a normal aorta.

The contraindications for intravenous abdominal aortography are the same as for angiocardiography.

Seven roentgenograms. J. DUDLEY KING, M.D.
Crawford W. Long Memorial Hospital
Atlanta, Ga.

TECHNIC

A Universal Planigraph. R. Janker. Fortschr. a. d. Geb. d. Röntgenstrahlen **73:** 253–261, July 1950. (In German)

The author describes a model of a planigraph which he constructed—a modification of the Gebauer-Wachsmann apparatus. The disadvantage of the latter lies in the fact that it cannot be used for patients who are unable to stand erect or to tolerate rotating motions.

Janker shows that to obtain horizontal body-section roentgenograms by the method of Gebauer-Wachsmann the patient and cassettes need to be rotated only 180 degrees. It thus becomes possible to obtain a planigraphic roentgenogram of a patient in a recumbent position by a simple improvement of the equipment, changing the tubestand to permit a maximum of 180 degrees motion, instead of the previous 30 or 50 degrees. The cassette is not attached to the stand, but to a separate horizontal bar which permits motion in different directions.

Even longitudinal planigraphic roentgenograms can be obtained by this method, with the patient in a horizontal, upright, or oblique position.

Six roentgenograms; 11 photographs.

EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

RADIOTHERAPY

Nasopharyngeal Malignant Tumor. An Overlooked Condition. Harold L. Hickey. Arch. Otolaryng. **53:** 53–66, January 1951.

Nasopharyngeal neoplasms have been said to represent more than 3 per cent of cancers of the upper alimentary and respiratory tracts and 0.2 per cent of all malignant growths (Martin: Cancer of the Head and Neck. New York, American Cancer Society, 1949). While all ages are subject to the disease, the greatest incidence is between the ages of forty-one and sixty years. Males are predominantly affected, and the Chinese race appears to be particularly susceptible.

The major cell types are: squamous-cell carcinoma, lymphosarcoma, lymphoepithelioma, and transitional-cell carcinoma, although quite often these distinctions are arbitrary.

The easy and rapid spread of the disease often obscures the diagnosis by causing the first manifestation to be outside the nasopharynx, such as a cervical mass, ophthalmoplegia, ear symptoms, and involvement of the cranial nerves. Horner's syndrome may result if the sympathetic plexus around the internal carotid artery is affected.

Early symptoms include otalgia, stuffiness in the ear, deafness, and tinnitus due to eustachian tube obstruction. A symptom complex of deep-seated pain in the fronto-temporal region, tinnitus, deafness, otalgia, a mass in the neck, and evidence of involvement of the 2nd, 3rd, 4th, 5th, 6th, 9th, 10th, and 12th cranial nerves, has been described (Figi: Wisconsin M. J. **46:** 611, 1947). Ophthalmologico-neurological symptoms are common. Nasal bleeding and nasal obstruction may occur but are believed by the author to be more characteristic of a sarcoma than of carcinoma. Any patient presenting any of the symptoms enumerated above, including ophthalmoplegia and evidence of trigeminal neuralgia, should be suspected of harboring a nasopharyngeal tumor.

Biopsy is mandatory but is often difficult, especially with small tumors, because of their relative inaccessibility. Roentgenograms, particularly in the verticomental projection, are often helpful and may show enlargement of the sphenoid foramina, destruction of the petrous tip, and erosion of the basiocciput or of the mesial portion of the greater wing of the sphenoid. Soft-tissue masses may also be demonstrated in the lateral view.

Treatment is by fractionated doses of deep roentgen therapy through several ports. The five-year survival rates range from 17 to 30 per cent, with lymphosarcoma and lymphoepithelioma seeming to have the better prognosis.

The author reports 24 cases. Initial symptoms were aural, including otalgia, deafness, tinnitus, and fullness, in 54 per cent; cervical swelling in 42 per cent; and ocular (ptosis or diplopia) in 38 per cent.

In 22 cases of the series receiving roentgen therapy, the five-year survival rates are incomplete. Seven patients were alive at the time of the report, but only 3 of these for five or more years after admission.

Five illustrations, including 1 roentgenogram.

CORNELIUS COLANGELO, M.D.
Chicago, Ill.

Cancer of the Tongue. Arthur G. James. Ohio State M. J. **46:** 1184–1185, December 1950.

Cancer of the tongue is said to cause more deaths than any other cancer of the head and neck. It is second only to cancer of the lip among malignant growths in or about the oral cavity.

Biopsy should always be done on any chronic ulcer or indurated area in the tongue. The possibility that the lesion may be syphilitic is no justification for delay in obtaining a specimen for histologic study.

Treatment depends on the type of cancer and its location and on the presence or absence of metastatic cervical nodes. Adenocarcinomas, sarcomas, and other radioresistant lesions should be treated by surgical eradication whenever possible. In the main, however, cancer of the tongue is epidermoid in type, and usually radiosensitive. Radiation therapy, external and/or interstitial, is indicated for this type of lesion in the base of the tongue. In the middle or anterior third either surgery or radiation is used, with radiation giving a better functional result.

Cervical node metastases are best treated by radical

dissection. At times a block removal of the primary tumor, part of the mandible, and the cervical nodes is done.

ZAC F. ENDRESS, M.D.
Pontiac, Mich.

Cancer of the Breast: Results of Treatment, 1929 to 1943. Jørgen Saugmann-Jensen and Paul Jacoby. Acta radiol. **34**: 453–468, December 1950.

The five-year survival period in carcinoma of the breast gives very little information as to permanent recovery. Metastases become evident quite late. Consequently, although statistics for survival with various modes of therapy are quite plentiful, their validity is always open to question.

McWhirter's series (Brit. J. Radiol. **21**: 599, 1948) is quoted among others: 790 cases treated by radical operation and postoperative roentgen therapy, with 32.4 per cent survival after five years, and 459 cases of simple mastectomy and postoperative roentgen therapy, with 42.9 per cent five-year survival. It is pointed out, however, that the radical series was treated in 1935–40 and the local operation series in 1941–42, and the suggestion is made that a more favorable selection in the later period may help to explain these figures.

The authors' own series of 289 cases treated by radical operation with preoperative and/or postoperative roentgen therapy at the Radium Center in Odense, Denmark, showed a 40 per cent five-year survival (34 per cent without symptoms). This is contrasted with a series of 41 cases with local operation and roentgen therapy showing a 66 per cent five-year survival. However, the latter series is admittedly small and selected for absence of axillary metastases. A ten-year follow-up in the former group (145 patients) showed only 18 per cent alive and well.

It is concluded that radical surgery in carcinoma of the breast offers a cure rate of only 20 to 30 per cent. Yet radical operation may be unnecessary if there are no axillary metastases, and either futile or dangerous if these are present. It is, in all instances, mutilating. The value of preoperative or postoperative roentgen therapy is not as yet definitely established. A plea is made for more flexible application of our present therapy methods and individualizing of treatment.

Seven tables.

JOHN F. RIESSER, M.D.
The Henry Ford Hospital

Treatment of Mixed Tumors of the Kidney in Childhood. Robert E. Gross and Edward B. D. Neuhauser. Pediatrics **6**: 843–852, December 1950.

Mixed tumors of the kidney in infancy and childhood can be easily recognized in most instances by physical and roentgen examinations. In general, it is not difficult to differentiate such tumors from other masses which may appear in the upper quadrants of the abdomen. Roentgen examination should include an intravenous pyelogram to determine the presence and condition of the opposite kidney and also to gain information regarding the mass and its relation to the ipsilateral kidney. With an embryoma, it is unusual to have no excretion of dye on the affected side; the renal pelvis can usually be visualized either within the shadow of the mass or pushed to its periphery. The kidney pelvis is apt to be greatly distorted and also displaced forward or backward, upward or downward, medially but seldom laterally. Intravenous pyelography usually gives all the information which is required; if it is not satisfactory, retrograde pyelograms should be made. In the presence of an abdominal neoplasm, it is necessary to search for metastatic lesions. Embryomas metastasize primarily to the lungs; neuroblastomas have a greater predilection for invasion of the skeleton, with involvement of the lungs only late in the course of the disease.

Treatment in all cases of kidney tumor should include transabdominal nephrectomy and postoperative roentgen irradiation to the area. At the Children's Hospital, Boston, from 1940 through 1947, 38 children with kidney tumors were treated, with a survival of 47 per cent; in babies under twelve months of age there were 80 per cent survivals. During the preceding nine-year period, 31 cases had been treated, with a survival of 32 per cent. Essentially, the surgical procedures were the same in the two groups, though the patients in the later group may perhaps have been seen a little earlier. The 1940–1947 group differs from the one of 1931–1939 primarily in the fact that postoperative irradiation was given in all but 2 cases.

It is the authors' practice to begin irradiation immediately after completion of the operation, before the patient recovers from the anesthesia. Treatments are given in daily doses of 200 r, alternately using three portals, anterior, lateral and posterior over the tumor bed, for a total of 4,000 to 5,000 r (measured in air), employing a 200-kv. machine, filters of 1 mm. of aluminum and 0.5 mm. of copper, with a target-skin distance of 50 cm., and a half-value layer equal to 1.05 mm. Cu.

Eleven patients in the 1940–1947 series were given some irradiation over the chest; in 3 patients this was done because of obvious pulmonary metastases, in 1 because of a widened mediastinal shadow which might have represented tumor, and in 7 because examination of the nephrectomy specimen showed tumor in veins, and it was thought desirable to attempt to kill off any cells which might already have seeded to the lungs. The authors are skeptical about what has been gained by the treatments over the thorax.

Whether preoperative irradiation has any advantage other than reducing the size of the mass and facilitating its operative removal is still unproved in the authors' experience or on the basis of any statistics that have appeared to date.

Two roentgenograms; 3 photographs; 2 tables.

Rectal Tumors of Doubtful Malignancy. A Personal Observation. Germain Pinsonneault. J. Canad. A. Radiologists **1**: 72–74, December 1950. (In French)

Malignant tumors of the rectum and anal canal are usually adenocarcinomas or squamous-cell carcinomas. Rarely a carcinoid tumor or basal-cell carcinoma is seen. The latter two types are of relatively low malignancy. Treatment of carcinoids is chiefly surgical. Since the tumor is usually less malignant in younger people and relatively more malignant in older people, it is recommended that the treatment be less radical in the young. The author also suggests that some of these might receive radiotherapy, although he presents no cases.

A case of basal-cell carcinoma of the lower rectal ampulla treated by roentgen irradiation is reported. The tumor and symptoms disappeared, and the treatment was considered successful. However, the period of survival after therapy is not stated.

CHARLES NICE, M.D.
University of Minnesota

Hodgkin's Disease. Herman A. Hoster. Am. J. Roentgenol. **64:** 913–917, December 1950.

If palliation is the sole aim in Hodgkin's disease, the problem of treatment requires no extensive discussion. If, however, the aim of the therapist is prolongation of life by active therapy, especially in the subacute and chronic forms of the disease, there is much to be said with respect to indications for and methods of treatment.

The response of the patient to treatment is materially affected by a number of factors: (1) the site of localization or principal area of disease involvement, (2) the rate of progress of the disease, (3) the stage of the disease at the time of therapy, (4) the degree of dissemination, (5) the age of the patient, and (6) the presence or absence of unfavorable extrinsic influences.

Involvement of the liver, spleen, and abdominal cavity causes a poorer outlook. The most chronic disease responds best and the most acute least, or not at all, with gradations in between. Unfavorable extrinsic influences include cellular inflammation and repair, as in burns, fractures, surgery, childbirth, and chronic infections. Physical exertion with fatigue and alcohol seem to exert deleterious effects.

Nitrogen mustard is indicated when the symptoms or signs indicate diffuse involvement. The author does not believe that this agent should be withheld until radioresistance is present. J. DUDLEY KING, M.D.
Crawford W. Long Memorial Hospital
Atlanta, Ga.

Obstructing Intrabronchial Hodgkin's Disease. Case Report. John F. Higginson and Jerome T. Grismer. J. Thoracic Surg. **20:** 961–967, December 1950.

The second recorded case of obstructive endobronchial tumor proved ante mortem to be Hodgkin's disease is here reported. The patient sought relief for pneumonitis secondary to obstruction. Antibiotics cleared the infection but residual atelectasis led to bronchoscopy and suspicion of bronchogenic carcinoma. Later a supraclavicular node biopsy and still later a repeat bronchoscopic biopsy demonstrated Hodgkin's disease. There were no other findings to suggest the correct diagnosis.

Response to x-ray therapy was very satisfactory, with complete re-expansion of the lung. In thirty-one days 1,800 r were given to the right anterior chest, 1,800 r to the right posterior chest (crossfiring the mass in the right hilus), and 1,500 r over the area of the lymph node biopsy. At the time of the report the patient had been followed for four months.

Two photomicrographs.

DONALD DEF. BAUER, M.D.
St. Paul, Minn.

Leukemia, Polycythemia and Related Diseases. Claude-Starr Wright. Am. J. Roentgenol. **64:** 907–911, December 1950.

The author reviews briefly our present knowledge of polycythemia vera and leukemia. After nine years experience with radioactive phosphorus, he believes it is the agent of choice in the treatment of polycythemia. Venesection is used freely early in the treatment to give symptomatic relief, since the maximum effect of the phosphorus therapy will not be reflected in the peripheral blood before forty to sixty days. In the average case 3 millicuries of radioactive phosphorus in the form of sodium dihydrogen phosphate is given orally, and observations of the hematologic response over the following two or three weeks are made before additional therapy is instituted. Individualization of treatment to each patient is imperative. The potential complications must also be kept in mind. Of these, the most important are intravascular thrombosis and hemorrhage.

Leukemia victims may live long enough to die of other diseases. Roentgen irradiation is still the prime therapeutic measure in chronic leukemia. Radioactive phosphorus, nitrogen mustard and urethane have proved helpful in some selected cases. In the management of acute leukemias, the addition of the folic acid antagonist—notably aminopterin—to the therapeutic armamentarium represents the greatest advance. For the first time we see evidence of a specific molecule inhibiting one specific strain of leukemic cells.

J. DUDLEY KING, M.D.
Crawford W. Long Memorial Hospital
Atlanta, Ga.

Diagnosis and Treatment of Lymphoblastoma and Leukemia from the Standpoint of the Radiologist. Joseph L. Morton. Am. J. Roentgenol. **64:** 919–928, December 1950.

The author believes that patients with leukemia and Hodgkin's disease should be treated by their own local medical groups whenever possible. This is more economical and simplifies the problem of adjustment to the disease. Errors of diagnosis and management can best be avoided by combined efforts of a group of physicians considering all the aspects of the condition. Roentgenographic survey will usually indicate the most efficient diagnostic approach; aspiration biopsy, exploratory operation, or other means of laboratory or clinical differentiation. Diagnosis by irradiation, the so-called therapeutic trial, is mentioned only to be condemned. The best results in non-leukemic lymphoma are obtained by the application of at least 2,000 r to the tumor and contiguous lymphatics, using fields that in so far as possible avoid normal tissue. A dose of this magnitude may be disastrous in some infectious diseases and certainly impairs resistance in those situations where radiation is of no proved value.

The location of involved visceral areas is often difficult, but valuable information can be elicited by roentgenographic examination, including the administration of contrast material when indicated. The lymph nodes of chronic lymphatic leukemia and the frequently found smooth mediastinal sheath of acute lympho-leukosarcoma have a much more flexible appearance with respiration than does the mediastinal infiltration of Hodgkin's disease or Boeck's sarcoidosis. Early involvement in the para-aortic nodes is not demonstrable by present-day methods. This involvement should be suspected as an area of renewed activity in Hodgkin's disease when symptoms are present and all methods to demonstrate an active focus fail to reveal the site. In the instances where the process has extended through the capsule of hilar lymph nodes, producing peribronchial accentuation or early atelectasis, regression is frequently less satisfactory. Such peribronchial infiltration indicates neglected late disease with a less favorable prognosis. After a trial of chemotherapy, continued manifestations in the peribronchial areas should be considered active Hodgkin's disease and vigorously treated. Procrastination results in irreparable damage to the lungs with secondary bronchiectasis. Involve-

ment of the bone or nervous system is usually a late occurrence in Hodgkin's disease, but when nervous system involvement does occur, accurate localization is imperative. Myelography of the spinal canal is safer than reliance on clinical localization for a site of infiltration or pressure.

Localized lymphosarcomatous lesions are treated up to skin tolerance. Management of local complications in leukemia is directed toward symptomatic relief without an attempt to control generalized cellular manifestations. Daily blood counts are essential during treatment, to avoid over-irradiation. It must be borne in mind that the count will usually decline for a few days after cessation of therapy. Giant follicular lymph node hyperplasia is controlled by therapy similar to that employed in Hodgkin's disease.

Nineteen roentgenograms.

J. DUDLEY KING, M.D.
Crawford W. Long Memorial Hospital
Atlanta, Georgia

Evaluation of Irradiation Therapy for Nonmalignant Uterine Bleeding at the University of Virginia Hospital. William N. Thornton, Jr., John M. Nokes, and Dwight J. Brown, Jr. Am. J. Obst. & Gynec. **61**: 75–79, January 1951.

The authors report on 348 cases of benign uterine bleeding treated by intracavity irradiation or by roentgen-ray therapy from 1925 to 1948, in which the initial pathological specimens were available. No evidence of malignant disease was found at the original examination. Ages ranged from twenty-four to eighty years. No patient younger than thirty-five years had been treated by irradiation after 1940. One hundred and seventy-eight patients were followed for varying periods between six months and ten years or more. In this group 26 non-malignant and 8 malignant complications subsequently developed. One half of the latter occurred ten or more years after the initial therapy. One patient died as a result of intracavity irradiation in the presence of an unrecognized pelvic tuberculosis.

The conclusion is reached that surgery is preferable to irradiation therapy in women forty years of age or younger. At the present time the authors reserve pelvic irradiation for those patients with benign endometrial bleeding requiring treatment, who have some contraindication to major surgery.

Six tables.

JOHN M. KOHL, M.D.
Jefferson Medical College

Management of Fibromyomata Uteri. C. H. Mauzy, F. R. Lock, and J. F. Donnelly. Am. J. Obst. & Gynec. **61**: 32–40, January 1951.

The present trend among gynecologists is stated to be toward a conservative management of uterine fibroids. The authors here seek to evaluate their own treatment. In a total of 4,077 gynecologic cases reviewed, 253, or 6 per cent, were diagnosed as fibroids. In 12 instances these were associated with pregnancy. In 153 cases (fibroids alone) hysterectomy was not advised but the patients were examined at regular intervals. Of this group 88 were followed, of whom 82 were improved (tumor stationary or decreasing in size and symptoms no longer present), including 28 treated by dilatation and curettage. Twelve myomectomies were done, and it was found that extensive surgery could be performed on a uterus without destroying its function. Only one of this group had a recurrence. Eight patients received irradiation for "flooding." All but one of the irradiated patients was considered well on follow-up examination.

Radical therapy, or hysterectomy, was recommended in 67 cases (26.4 per cent). A review of these cases indicated that in 26 cases operation was not wholly justified.

The 12 cases with pregnancy are considered separately. Six of these were treated conservatively; in 5 myomectomy was done either in association with cesarean section or as an incidental procedure, and 1 patient had a total hysterectomy, the pregnancy being an incidental finding.

It was felt that the conservative approach was best and that it could have been extended further with equally good results. Since irradiation works by suppression of the ovarian function, in the authors' opinion it should be avoided when possible.

Seven tables.

JOHN M. KOHL, M.D.
Jefferson Medical College

A Universal Diaphragm for Deep Roentgen Therapy. Olof Sandström. Acta radiol. **34**: 546–550, December 1950.

A step diaphragm is here described which utilizes the tool of field definition by visible light. A plane mirror is placed in front of the opening in the tube housing and reflects the light of a small lamp which is introduced into the field at a distance equal to the target-mirror distance. This makes possible a reduction in the size of the instrument. A compression plate is attached and lighting is accomplished with this in place. The author claims a sharp delimitation of the beam with this universal diaphragm.

Roentgenographic visualization of the treatment field is obtained with a Lysholm grid and a Hernheiser lattice on the skin.

Six figures.

JOHN F. REISSER, M.D.
The Henry Ford Hospital

Isodose Measurements of Linear Radium Sources in Air and Water by Means of an Automatic Isodose Recorder. Gerald J. Hine and Milton Friedman. Am. J. Roentgenol. **64**: 989–998, December 1950.

The Paterson and Parker gamma-ray dosage system is constructed mathematically on one confirmed calibration: 1 milligram hour exposure from a point source of radium filtered with 0.5 mm. platinum delivers, at a distance of 1 cm., an intensity of 8.4 gamma roentgens. For a simple linear radium source, the calculated intensity distribution for the gamma radiation coming from the sides is probably correct. The radiation field around the ends, however, can be obtained mathematically only with some approximations, due to the unknown self-filtration factor of radium and the complexity of evaluation of oblique filtration through the walls of the capsule. With the aid of a scintillation counter as a gamma-ray detector, together with an automatic isodose recording device, the radiation fields around various radium sources were surveyed by the authors by means of isodose curves and compared with those derived mathematically.

The scintillation counter overcomes some of the defects of the air ionization chamber. The radiosensitive part of the counter is a cylindrical calcium tungstate crystal 1/8 inch in diameter, 1/8 inch in height, with a volume of 0.03 c.c. Light flashes produced in the

crystal by the gamma-rays are conducted through a quartz rod to a photomultiplier, which converts the flashes into electric pulses that can be recorded.

Like the Geiger counter, the scintillation counter registers only a fraction of the incident gamma rays, and dosages cannot be determined directly. Therefore, the counter is calibrated by comparison with ionization chamber measurements.

Multiple isodose curves for various radium tubes singly and in tandem are recorded by the authors. In general, there is an excellent correlation between the isodose curves constructed mathematically and those obtained by actual measurement. However, measurements reveal that commonly employed radium tubes show an asymmetrical isodose pattern rather than the symmetrical one usually described, and multiple linear sources in tandem yield isodose curves dependent upon the position of the tubes relative to each other.

As a result of a comparison of air and water measurements, the authors also point out that close to the radium source the presence of a scattering medium, such as water, does not result in any significant change in intensity distribution, but at a point 3 cm. from a 1.5 cm. radium tube, an increase in intensity is observed due to the scattered gamma rays.

Eleven illustrations, including photographs, radioautographs, and isodose curves.

RICHARD A. ELMER, M.D.
Emory Medical School

Clinical Isodose Curves. R. Loevinger, B. S. Wolf, and W. Minowitz. Am. J. Roentgenol. **64:** 999–1009, December 1950.

The bulk of the depth dose data available to clinicians has been obtained by measurements along the central axis of the roentgen ray beam, in an infinite, homogeneous tissue-equivalent phantom. Since clinical depth doses may differ from these conventional values, due either to the finite size or unusual shape of the irradiated region or to the presence of bone or fat, the authors set out to find some useful generalizations which would serve to indicate the nature and extent of the deviations to be expected from the conventional central axis determinations and to simplify the determination of isodose curves in finite phantoms.

The measurements reported were made with a 200-kv. generator at 50 cm. focus-skin distance, with 0.4 mm. Cu plus 1.0 mm. added filtration, giving 1 mm. Cu h.v.l. Characteristics of the phantom material and necessary properties of the condenser ionization chamber are listed. The infinite phantom, *i.e.*, "so large that larger will not change the readings," is described and illustrated fully.

Using an infinite phantom, depth dose measurements were made both on and off the central axis, with rectangular and circular fields of various sizes. With a 10 × 15-cm. field, depth dose measurements were obtained on the central axis of the beam and along the lines 3, 5, and 7 cm. off axis and parallel to it. By plotting on semilogarithmic paper the percentage depth doses against the depth in centimeters, it was noted that for depths below 4 cm. the central axis depth dose curve is a straight line, and the off-axis depth dose curves are accurately parallel to it. This means that the depth dose curve along any line parallel to the axis may be obtained by multiplying the central axis curve by a constant. Moreover, the value of this constant is not a function of the depth, but only of the distance from the central axis.

Similar semilogarithmic plotting with the semi-infinite phantom (*i.e.*, a phantom infinite in all directions except in thickness) revealed considerable information. For example, the depth dose may be considered to be made up of three components: the primary beam, the forward-scatter, and the saturated back-scatter of the infinite phantom. Graphs of these various components show that, in general, the difference between the exit dose curve and the primary beam curve, at a given depth, represents the dose due to forward-scatter at that depth.

Phantom measurements have been similarly applied using a water filled 1/16-inch acrylic plastic phantom made to conform to the size and shape of the human neck. These studies were valuable in estimation of dosage in the treatment of carcinoma of the larynx.

The paper is well illustrated with graphs and isodose curves and merits careful study for thorough understanding.

Fourteen illustrations, including graphs, and isodose curves.

RICHARD A. ELMER, M.D.
Emory Medical School

RADIOISOTOPES

Diagnostic and Therapeutic Use of Radioactive Iodine. Dwight E. Clark, Otto H. Trippel, and Glenn E. Sheline. Arch. Int. Med. **84:** 17–24, January 1951.

Radioiodine has proved to be a valuable agent in the diagnosis of thyroid function. The methods involve the determination of the rate of urinary excretion, uptake by the thyroid gland, and incorporation into the "hormonal" iodine of the blood.

The mean urinary excretion in thyrotoxic patients has been placed at 25 per cent (McArthur *et al.*: Ann. Int. Med. **29:** 229, 1948. Abst. in Radiology **53:** 154, 1949), with a range of 7 to 45 per cent, while in euthyroid patients the average excretion is 59 per cent, with a range of 23 to 98 per cent. The excretion by hypothyroid patients varies from 75 to 95 per cent.

Measurement of the rate and extent of uptake by the thyroid gland following a small dose of I^{131} was studied by Werner, Quimby, and Schmidt (J. Clin. Endocrinol. **9:** 342, 1949. Abst. in Radiology **54:** 474, 1950). They found that 91 per cent of the euthyroid patients had an uptake between 10 and 35 per cent. The other 9 per cent had higher values. Ninety-four per cent of their hyperthyroid patients had uptakes greater than 35 per cent. The remaining hyperthyroid patients showed 34 per cent uptake or under.

The rate of incorporation of injected radioiodine into plasma protein-bound iodine varies with the degree of thyroid activity. By determining the total amount of radioiodine in the plasma and the amount in the plasma protein twenty-four hours after the ingestion of 1.0 to 1.5 millicuries of I^{131}, the conversion ratio can be calculated. This is defined as

$$\frac{\text{Protein-bound plasma } I^{131}}{\text{Total plasma } I^{131}} \times 100$$

Normal values as determined by Clark, Moe, and Adams (Surgery **26:** 331, 1949. Abst. in Radiology **55:** 317, 1950) ranged from 13 to 42 per cent in 22 euthyroid

patients and from 45 to 96 per cent in 28 patients with hyperthyroidism.

During a period of thirty-two months the authors treated more than 200 patients having hyperthyroidism. In 100 of these, therapy had been completed at the time of this report. A dose of approximately 0.1 millicurie per estimated gram of thyroid tissue was given. If the initial dose was inadequate, additional radioiodine was administered. Of the 100 patients in whom therapy was completed, 88 had a satisfactory remission; hypothyroidism developed in 9, and 3 became myxedematous. Persons with diffusely enlarged thyroid glands required an average of 5.6 millicuries of I^{131} and patients with toxic nodular goiters needed an average of 11.7 millicuries.

In the treatment of thyroid carcinoma the first step is to remove the thyroid surgically or destroy it with I^{131}. This is done to increase the uptake of radioiodine by the remaining malignant tissue. Thirty-five millicuries of I^{131} is administered orally every two weeks until there is no longer localization of I^{131}, as determined by external survey with a Geiger-Müller tube.

Data on 50 patients with local invasion and/or metastases from thyroid carcinoma treated in this manner are presented. Thirty-eight per cent of the number had died. The histopathological studies in all of these revealed either a papillary adenocarcinoma or an undifferentiated carcinoma. Thirty-one patients were still living. In 30 per cent of these, the neoplasm concentrated the isotope; 8 showed a good response to therapy. Histologically these growths were of the alveolar and follicular type.

Seven other patients with Hürthle-cell, predominantly papillary or solid types of carcinoma were still living, but these tumors had shown no avidity for radioiodine.

Two roentgenograms.

HOWARD L. STEINBACH, M.D.
University of California

Radioactive Iodine in the Treatment of Hyperthyroidism. E. Perry McCullagh and Charles E. Richards. Arch. Int. Med. **87**: 4–14, January 1951.

The results of I^{131} treatment in 203 patients having diffuse goiters and hyperthyroidism and in 78 patients having nodular goiters and hyperthyroidism are presented.

All but 16 of the 203 patients with diffuse toxic goiters were in remission when last seen. Four of the 16 cases not in remission were known to have hyperthyroidism six months or more after their initial treatment.

Patients with diffuse toxic goiters with a greatly elevated basal metabolic rate required a dose of I^{131} approximately 15 per cent higher than those with low rates. There was a close relationship between the size of the thyroid gland and the dose requirement. The recurrence rate was 3 per cent.

Of the 78 patients with nodular goiter, 18 remained hyperthyroid. The severity of hyperthyroidism in these patients bore no relationship to the size of the dose required for remission. There was a closer relationship between the size of the gland and the dose necessary, but this was less definite than in toxic diffuse goiter. The total dose required to produce a remission of the disease was much higher for nodular goiter than for toxic diffuse goiter.

Hypothyroidism has been the only complication encountered, having occurred in about 10 per cent of the patients with diffuse toxic goiter. No case of hypothyroidism in a patient having toxic adenoma treated with radioactive iodine has yet been observed.

Two charts; 12 tables.

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Radioactive Iodine for Hyperthyroidism Administered During Early Pregnancy. John E. Clever. Am. J. Obst. & Gynec. **61**: 217–219, January 1951.

One case is reported of hyperthyroidism treated with radioactive iodine during pregnancy.

The patient had a thyroidectomy in 1946 for hyperthyroidism. In January 1949, she had a course of thiouracil for recurrence of symptoms, but the drug was discontinued because it was poorly tolerated. In April 1949, she received 5 mc. of I^{131}. At that time she had been amenorrheic for ten weeks, and she was subsequently found to be pregnant.

On Nov. 11, 1949, the patient was delivered of a male infant weighing 5 pounds, 12 ounces. The postpartum course was uneventful. The basal metabolic rate had fallen from +32 to +3. The infant appeared slightly immature but showed no abnormalities, and developed normally emotionally and physically up to the last examination reported, at five months of age.

The author comments on the possibility of fetal damage due to exposure to radiation, mentioning the induction of neoplasm, production of blood dyscrasias, genetic changes, shortening the span of life, athyrotic cretinism, and possible stimulation of compensatory thyroid hypertrophy and overproduction in the presence of maternal hypothyroidism.

Views of various investigators regarding uptake of iodine by the fetal thyroid gland are given.

MASON WHITMORE, M.D.
Jefferson Medical College

Radioactive Iodine Studies Following Hemithyroidectomy for Carcinoma of the Thyroid. A Possible Aid in the Diagnosis of Early Metastases. A Case Report. Kenneth R. Crispell. Virginia M. Monthly **77**: 652–654, December 1950.

The author reports the case of a 32-year-old white female who had had a hemithyroidectomy for carcinoma of the thyroid gland. Subsequently, cervical adenopathy developed and radioactive iodine tracer studies were done. The data obtained indicate the difficulty encountered in evaluating tracer studies for early metastases in cases where functioning thyroid tissue remains in the neck.

RODERICK L. TONDREAU, M.D.
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Concerning Treatment by Radioactive Iodine of Cancer and Metastases of Thyroid Origin. J. Chester, P. Lerch, and A. Vannotti. Schweiz. med. Wchnschr. **80**: 1377–1381, Dec. 30, 1950. (In French)

A 47-year-old female was subjected to subtotal thyroidectomy for carcinoma in 1949. A year later metastases were discovered in the lungs, skull, humerus, scapula, and pelvis. Therapy with radioactive iodine was attempted. At first, Geiger counts over the thyroid were normal, but with subsequent therapeutic doses the Geiger counter revealed diminished activity. The iodine was taken up by the thyroid but after eight hours

the count diminished rapidly, indicating that the iodine was not retained long enough to form thyroxin, which in turn indicated an essentially non-functioning thyroid. Retention in the metastatic areas was also brief, showing a rapid drop after six to eight hours.

The authors conclude that the thyroid gland should be completely removed before one attempts treatment of metastases by radioactive iodine, and that such therapy of the metastases will not be effective if the metastatic areas are only "partially functioning."

Two roentgenograms; 3 graphs.

CHARLES NICE, M.D.
University of Minnesota

Blood Volume in Polycythemia as Determined by P^{32} Labeled Red Blood Cells. Nathaniel I. Berlin, John H. Lawrence, and Jean Gartland. Am. J. Med. **9**: 747–751, December 1950.

The blood volume was determined with P^{32} in 53 cases of polycythemia vera, 6 cases of secondary polycythemia, and 7 cases of relative polycythemia.

Polycythemia vera: (1) Thirty of 32 patients with a hematocrit of 55 or greater had elevated total red cell volumes; 22 had low plasma volumes; 8 were under the average and 2 above average. All, however, were within the normal range. One patient showed an increased plasma volume. (2) Of 9 patients with hematocrits of 50 to 54 inclusive, 7 had elevated total red cell volumes; the other 2 patients had low plasma volumes, resulting in falsely high hematocrits. (3) The 12 patients with hematocrits under 50 had normal or low total red cell volumes. There were 3 patients with low and 1 with a high plasma volume.

Secondary Polycythemia: The 5 untreated patients in this group had elevated total red cell volumes and low plasma volumes.

Relative Polycythemia: The patients in this group had normal total red cell volumes but high hematocrits due to an unexplained low plasma volume.

On the basis of these observations, it is concluded that the absolute polycythemias can be differentiated from the relative polycythemias by blood volume determinations. Secondary polycythemias, however, cannot be differentiated from polycythemia vera by this means.

The total red cell volume cannot be predicted from the hematocrit. There is a direct correlation (0.75) between the total red cell volume and the number of circulating white blood cells.

Two charts; 1 table.

The Effect of Radioactive Phosphorus Upon the Development of the Embryonic Tooth Bud and Supporting Structures. M. S. Burstone. Am. J. Path. **27**: 21–31, January-February 1951.

Administration of P^{32} to pregnant mice was found to result in disturbances of osteogenesis and odontogenesis in the offspring. The dosages required to produce these changes are less than are required to produce similar changes in immature mice.

Twelve photomicrographs.

Circulatory Transfer of P^{32} to Skeletal Muscles Under Various Experimental Conditions. D. L. Gilbert, C. D. Janney, and H. M. Hines. Am. J. Physiol. **163**: 575–579, December 1950.

A study was made of the amount of P^{32} uptake by the gastrocnemius muscles of adult rats under various experimental conditions, in which one limb served for the experiment and the contralateral limb as its control. The muscles were removed for study thirty seconds after an intraperitoneal injection of 0.4 millicuries of P^{32}.

The P^{32} uptake was the same in the right and left gastrocnemii of normal control animals. Vigorous tetanic contraction of muscle was accompanied by a decreased uptake of P^{32}, whereas during the period of relaxation and recovery the uptake was greater than in the controls. Immobilized muscles took up less P^{32} than their controls. The total phosphate uptake was unaffected by tenotomy, but the uptake on a gram-weight basis was increased. Denervation was followed by a decreased uptake of P^{32}, the amounts of which roughly paralleled the degree of atrophy. However, in the longer periods of atrophy the uptake per gram was found to be increased. The condition of prolonged shortening or spasticity in muscle was accompanied by a decreased uptake of P^{32}. This effect was abolished by deep anesthesia and lessened by daily treatments with stretching. It is postulated that a reduced effective circulatory transfer may contribute to the atrophy and functional impairment found in spastic muscle.

Five charts.

Distribution of Radioactive Gold Colloid in Rats, Mice, and Transplanted Mouse Tumors. G. Z. Williams, A. C. Stanton, R. M. Jamison, and J. T. Williams. South. M. J. **43**: 1031–1037, December 1950.

An investigation to determine the effects of internal radiation of cancer by radioactive gold colloid has been carried out by the authors, who report here their preliminary results.

Radioactive gold sol was injected into a total of 287 mice and 40 rats in tracer doses of 20 to 100 microcuries and therapeutic doses of 1 millicurie per animal. Administration was by intraperitoneal, intracardiac, and intrasplenic injections, as well as by subcutaneous and tumor infiltration. Blood samples were removed and counted with a Geiger-Müller tube and scaler. The animals were sacrificed and fixed blocks of tissue were sliced, dried, and counted.

With administration by the intravenous or intrasplenic route, 95 per cent of the radioactive gold was deposited in the liver and spleen, being retained by the Kupffer and reticulo-endothelial cells. When the isotope was injected locally into tumors of mice, the greatest portion (80–100 per cent) remained in the tumor. Uniform distribution of the gold colloid in solid tumors was very difficult to obtain by needle infiltration.

Satisfactory regression of transplanted sarcomas was obtained by injections of 200 to 400 microcuries of the isotope, with careful infiltration. In some cases poor distribution of the material resulted in partial regression, with subsequent marginal recurrence.

Experiments were also conducted to determine the effects of chemotherapeutic agents and radioactive gold on transplanted sarcoma 180. Nitrogen mustard alone resulted in 42 per cent regression; gold alone effected 68 per cent disappearance of tumors; the effects of nitrogen mustard and colloidal Au^{198} in combination were additive, with a regression rate of 82 per cent.

Nine illustrations.

ROBERT H. LEAMING, M.D.
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RADIATION EFFECTS

On the Roentgen Tolerance Dose. H. Wilhelm Ernst. Fortschr. a. d. Geb. d. Röntgenstrahlen **73:** 362–370, July 1950. (In German)

At present there is great confusion as to the maximum tolerance dose of roentgen rays because the various ideas upon which it is based are not identical. Twelve tolerance doses are mentioned in this report, including 0.3 r per week in the United States, 0.1 r in Sweden, and 0.5 r in Great Britain. In Germany the permissible maximum dose for an eight-hour day was established as 0.25 r (0.025 r for the abdomen) by the German Industrial Commission (Berufsgenossenschaft für Gesundheitsdienst und Wohlfahrtspflege) in 1940. This, however, is a peak level and not a permissible average dose.

Ernst discusses the various points of view and offers certain definitions or suggestions for expressing the tolerance dose:

1. The *genetic-damaging dose* should be an integral dose expressed in r. The lower time limit for such a dose lies before birth; the upper time limit is that period in which no damage to offspring is possible or could be anticipated.

2. The *general damaging dose* should be a threshold dose giving that amount of radiation which objectively does not damage a human being. For some organs this figure might be zero; for others it would be relatively high.

3. The *tolerance dose* is that amount of radiation which a human being could tolerate without subjective damage. It would be higher than the threshold dose mentioned above and would vary for different organs.

4. The *tolerance intensity* would be that dose rate which would be tolerated uninterruptedly (24 hours per day, seven days a week). Ernst doubts that such a dose exists in reality.

5. *Permissible average dose.* Simplification of such a figure would be necessary and Ernst suggests distinguishing between soft and hard rays.

6. *Permissible average intensity.* Here again a distinction should be made between hard and soft rays. The intensity should be expressed in r per life, year, week, day, hour, and minute.

7. *Maximum permissible dose.* It is suggested that a distinction be made between rays used in therapy and diagnosis and that figures be given for general body radiation, exposure to the hands, and to the lower abdomen.

8. *Actual maximum irradiation.* Here individualization is suggested, with consideration of the radiation protection for each installation. The actual highest amount of the tolerance dose should be expressed in r per day.

9. *Average dose intensity.* This is recommended for legal purposes after calibration of the individual unit and consideration of the actual working conditions.

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Tolerance Dose Problems in Radiological Work. P. Bjerre Hansen and C. B. Madsen. Acta radiol. **34:** 519–528, December 1950.

The authors review the work which has been done in Sweden and elsewhere on the so-called "permissible dose" of radiation and report a study of their own carried out at the Radium Center and Municipal Hospital, Aarhus. For the purposes of this investigation, film badges were believed to offer sufficient accuracy for determination of total body irradiation.

Hematological studies every three months and regular film badge determinations by densitometric means were carried out for a period of fifteen months on three groups of workers, comprised respectively of personnel from the Departments of Radium Therapy, Roentgen Therapy, and Diagnostic Radiology, with a fourth group of non-exposed personnel (photographers and maids) as a control. The protective measures followed the usual lines.

The results of the hematological examinations are presented graphically. Only the Radium Therapy personnel revealed minor changes in the form of a moderate tendency to anemia and slight leukopenia. The exposure of these workers was shown by the film badge measurements to be about 25 times as great as for the other groups.

Assuming a tolerance dose of 100 mr per day, the average exposure of the radium workers was at the upper limits of the tolerance range, but in some 15 per cent of the group the accepted value was considerably exceeded, exposures reaching 200 or 300 mr per day. Roentgen therapy and diagnostic personnel, as well as the control group, showed an average well below 20 mr per week.

Proposals for more cautious radium handling and better protection are advised. The authors favor a reduction in the tolerance dose to 100 mr per week.

Illustrated by graphs. JOHN F. RIESSER, M.D.
The Henry Ford Hospital

Do Children Born of Offspring of Mothers Irradiated for Sterility Show Abnormal Genetic Effects? Ira I. Kaplan. Arch. Pediat. **67:** 569–572, December 1950.

The author reports three instances of normal children born of individuals whose mothers had been irradiated for sterility. He points out in this connection that in the reported instances of abnormal children born to mothers treated by x-rays, the treatment was not given for sterility.

In one of the 3 cases reported the irradiation was given to the ovaries and to the pituitary, and in 2 instances to the ovaries alone. In all 3, normal progeny resulted, who developed normally and in the usual course of events produced three apparently normal second generation offspring.

No data are given as to the amount of irradiation administered, but one can assume that the patients were treated in the manner described by the author elsewhere. HERBERT D. KERMAN, M.D.
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Lesions of External Auditory Canal. Walter P. Work. Ann. Otol., Rhin. & Laryng. **59:** 1062–1087, December 1950.

In this paper on lesions of the external auditory canal the author includes a section on the injurious effects of roentgen and radium irradiation. Only that part of his discussion is abstracted here.

It is uncommon for x-ray therapy to produce injurious changes in bone through intact soft tissues, as these tend to filter a certain amount of the damaging rays. Apparently, one notable exception is found in the external auditory canal, where bone lies close to

overlying skin. Damaging x-ray therapy is usually directed at other lesions in close proximity to the external auditory canal, such as carcinoma of the pinna, carcinoma of the nasopharynx, carcinoma of the face, or metastatic malignant nodes. To treat such neoplasms satisfactorily by roentgen therapy, the external auditory canal may of necessity be included in one of the portals used. Two cases are reported in which the dosage of x-ray therapy to the primary lesion was in excess of 4,000 r (in air). Several months following completion of the therapy, the patients complained of pain in the ear and foul otorrhea. Inspection showed the canal to be filled with a purulent exudate. When this was removed, bare bone could be seen and palpated in the bony canal wall inferiorly. The bone did not bleed with manipulation. No granulations formed on its surface. Epithelium about the bone appeared to be pearly and piled up. The epithelial borders bled readily with trauma, and pain was extreme on touch or pressure. The tympanic membrane was not noticeably involved by the therapy.

During irradiation therapy, changes in the vascular supply and marrow spaces of the bone may occur. If therapy is prolonged, aseptic necrosis of the bone will result. This in turn causes a denudation of the thin skin of the bony external auditory canal wall leading to chronic ulceration. If the portal of entry of the roentgen therapy is large and the dosage is sufficiently concentrated, the squama of the temporal bone and the head of the mandible may undergo aseptic necrosis.

Ulceration and bony necrosis can be alleviated only by wide surgical intervention. The end-result of radium emanation in bone is much the same as with x-ray therapy.

STEPHEN N. TAGER, M.D.
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Ocular Changes Produced by Total Body Irradiation. Helenor Campbell Wilder and Russell M. Maynard. Am. J. Path. **27:** 1–19. January-February 1951.

The object of the present study was twofold: (1) correlation of the changes in the eyes of experimental animals exposed to ionizing rays at Bikini with those in the eyes of atomic bomb casualties from Hiroshima and Nagasaki (conjunctival and intraocular hemorrhages and serous exudates; septic choroiditis; bacteria in the intra-ocular vessels) and (2) comparison of the ocular changes produced by atomic fission radiation with those produced by total body roentgen irradiation.

The material available for examination was derived from animals in three categories: (1) 21 goats and 31 pigs receiving varying amounts of total body ionizing radiations at Operation Crossroads; (2) 24 pigs receiving total body roentgen radiation and 4 fetuses from roentgen-irradiated sows; (3) 24 control animals. The swine used at Bikini were three to four months of age at the time of exposure; the goats, three to four years. The controls were herd mates of the irradiated animals and included some which had been aboard target vessels, but at too great a distance from the explosion to receive any calculated radiation. The 24 pigs subjected to total body roentgen irradiation were from a single herd and from twelve to fifteen months old at the time of exposure. With the exception of the fetuses, from which both eyes were taken, only one eye was obtained from each animal.

Pathologic changes in the eyes of experimental animals receiving total body irradiation from atomic fission were found to be similar to those resulting from roentgen irradiation. For the most part, they were regarded as results of bone marrow depression and secondary systemic changes, rather than as direct effects of the rays. The hemorrhages were attributed to thrombocytopenia and to the heparin-like substance demonstrated by Allen and Jacobson (Science **105:** 388, 1947). Serous exudates were the result of increased vascular permeability, possibly secondary to anemia. Septic choroiditis and bacteria in the vessels were manifestations of the septicemia. Vacuoles similar to those observed by Schlaegel (Am. J. Ophth. **30:** 127, 1947) were present in the lenses of many of the irradiated animals but were found also in the controls and therefore were not regarded as a specific manifestation of irradiation damage. Massive cataract in irradiated animals may have been due to direct irradiation, although secondary nutritional effects associated with the anemia and severe hemorrhages could not be ruled out. Immediate changes in the lens specific for irradiation were not apparent in the young or mature animal. Knowledge of latent changes must await further experimentation. Although the secondary effects of ionizing and roentgen radiation were similar in the eyes of both pigs and goats, there were no ocular changes which could be attributed unequivocally to direct irradiation.

Eleven photomicrographs.

Medical Aspects of Atomic Explosion. Heinz Richard Landmann. J. Kansas M. Soc. **51:** 557–562, December 1950.

Three kinds of effects are produced by an atomic explosion—blast, thermal, and radiation. The first two are the more important from the standpoint of producing casualties.

By far the greatest number of radiation casualties are caused by the delayed or residual radiations emitted by the fission products rising in the atomic cloud. The gamma rays, because of their long range, are most to be feared and may produce severe biological damage. Neutrons have a short range and are present for only an imperceptible period following the actual explosion of the bomb. Their danger is dependent upon their power of penetration, so that buildings and shelters of ordinary reinforced concrete afford no protection against them.

Radiation effects in both Hiroshima and Nagasaki accounted for 15 per cent of the casualties. The effects of various doses are listed as follows:

up to 25 r	No injury.
25–50 r	Possible blood changes.
50–100 r	Blood changes, some injury, no disability.
100–200 r	Definite injury, possible disability.
200–400 r	Definite injury and disability, death possible.
400–600 r	400 r lethal to 50 per cent. 600 r lethal to 100 per cent.

The uppermost problem in the management of radiation sickness is the maintenance of proper water balance. Therefore, intravenous saline and 5 per cent glucose should be used early. An adequate diet, supplemented by intravenous feedings, is also a requirement. Other measures which may be called for include the use of antibiotics, transfusions, control of hemorrhage by toluidine blue and protamine sulfate.

The paper concludes with a discussion of decontamination and protection of personnel working in bombed areas.

Two tables.

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Biochemical, Cellular, and Bacteriologic Changes in Thoracic Duct Lymph of Dogs Exposed to Total Body Irradiation. Crawford S. Brown, Esther Hardenbergh, and John L. Tullis. Am. J. Physiol. **163:** 668–675, December 1950.

Biochemical, cellular, and bacteriologic studies were conducted on thoracic duct lymph and blood in normal dogs and in dogs exposed to 500 r total body x-irradiation. Lymph total protein fluctuated within the first fifty hours after irradiation and then decreased at a slow, even rate. Uric acid and non-protein nitrogen levels in lymph increased within four hours following irradiation, but later decreased to slightly below normal. Lymph creatinine decreased within four hours following irradiation; after eighteen hours it rose gradually toward the normal level. Sugar and chloride levels showed no appreciable change. The total number of white blood cells in lymph dropped precipitously within four hours after irradiation, and remained at a low level throughout the period of observation. Bacterial cultures of blood and lymph were negative.

Three charts; 3 tables.

Effect of Roentgen Rays on the Testis: Quantitative Histological Analysis Following Whole Body Exposure of Mice. Allen B. Eschenbrenner and Eliza Miller. Arch. Path. **50:** 736–749, December 1950.

Previous studies of mice subjected to chronic, daily total body irradiation by 8.8 r, 4.4 r, and 1.1 r of gamma rays, while revealing a decrease in the total quantity of spermatogenic elements in the testes, showed a normal proportion between the cells in different stages of spermatogenesis (J. Nat. Cancer Inst. **9:** 133, 1948). Since cell death was minimal, it was assumed that the above changes were due to retardation of mitosis of spermatogonia.

In the experiments described here, the damage and recovery pattern of the testes following acute x-irradiation was studied. Different groups of mice were exposed to total body doses of 50 r, 100 r, 200 r, 300 r, and 400 r generated at 186 kv., and observations were made of the weights of the fresh testes and the quantitative histologic changes in the spermatogenic elements. This damage-recovery pattern was also studied in terms of weights of fresh testes following a 200 r total body dose, after recovery from an equal initial dose; and in terms of weights of fresh testes following exposure to a 10-mev source of x-rays for comparison with 186-kv. x-rays. These studies allow certain observations and conclusions:

1. The testes lose weight in direct proportion to the total body dose administered, due to the inhibition of division of spermatogonia to form daughter spermatogonia effected by the selective action of ionizing radiations on this stage of spermatogenesis alone. Cell death is not responsible. Partial inhibition probably occurs with 50 r doses, but with 400 r, inhibition is complete and lasts two to three weeks.

2. Resting spermatogonia present at the time of irradiation appear to develop normally into spermatocytes, spermatids, and spermatozoa.

3. The process by which the spermatogonia divide into daughter spermatogonia and the secondary spermatocytes into spermatids is generally considered to be morphologically the same as somatic mitosis in general.

4. The course of damage and recovery of the testis following exposure to a second dose of radiation is the same as that of damage and recovery following an initial exposure. This indicates complete metabolic recovery of spermatogenesis and suggests lack of development of "radioresistance." The observation that there is a difference in the sensitivity of these two cell divisions to ionizing radiation suggests that they are physiologically different, although morphologically similar.

5. The pattern of loss and recovery of weights of the testes of mice exposed to 10-mev roentgen rays is the same as that following exposure to 186-kv. roentgen rays.

6. The testis is a useful organ for measuring the biologic effect of ionizing radiations.

Five photomicrographs; 3 graphs.

CORNELIUS COLANGELO, M.D.
Chicago, Ill.

Effects of Roentgen Rays on Cancer. I. Direct Microscopic Observation on Living Intraocular Transplants of Frog Carcinoma. Balduin Lucké, and H. G. Schlumberger. J. Nat. Cancer Inst. **11:** 511–543, December 1950.

The experiments reported in this paper involved direct microscopic examination of living tumors growing in the anterior chamber of the eye and a study of the effect of roentgen rays upon these tumors.

For these studies retinal adenocarcinoma occurring in the frog (*Rana pipiens*) was employed. Well established tumor transplants were submitted (1) to irradiation with single doses of 2,000, 4,000, or 6,000 roentgens; (2) to repeated irradiation with small doses on alternate days—200, 400, 900, and 1,400 r respectively until a total of 3,200 to 15,600 r was reached. Radiation was supplied by a Chaoul tube employing 50 kv., with 0.2 mm. of copper filter, h.v.l. 2.4 mm. of aluminum.

Three main types of response were observed:

(1) Increasing granularity and opacity of the neoplastic outgrowths, probably due to flocculation and coagulation of intracellular colloids; shrinkage, fragmentation and ultimate disappearance of the most actively growing, non-vascularized parts of the tumor; progressive diminution in size and reduction of the tumor as a whole to a fibro-hyaline mass, or its complete disappearance. These regressive changes took place rapidly after a single large dose of 6,000 r, or more gradually after a single dose of 4,000 r. With repeated small doses of 900 or 1,400 r, a total of from 7,200 to 12,600 r was required to effect regression.

(2) A typical diphasic response. Gradual cessation of growth and onset of regression accompanied by progressive diminution in size for approximately four weeks; thereafter renewed and rapid regrowth of the neoplastic tissue. Such changes were observed after single doses of 2,000 r. The absence of residual irradiation effects was shown by the transplantability of the tumors at the end of the experiment.

(3) No perceptible effects. The tumors continued to grow in a normal, or perhaps somewhat accelerated, manner. This was the case when doses of 200 r were given on alternate days for a total of 3,200 r. The absence of any injury to the irradiated tumors was further demonstrated by their continued growth after retransplantation.

The observations are well documented by ten sets of serial photographs of intra-ocular implants. Three tables are also included.

DONALD S. CHILDS, JR., M.D.
The Mayo Clinic

Transparent-Chamber Observations of the Response of a Transplantable Mouse Mammary Tumor to Local Roentgen Irradiation. Ruth Merwin, Glenn H. Algire, and Henry S. Kaplan. J. Nat. Cancer Inst. **11**: 593–623, December 1950.

The authors report their studies on the effects of ionizing radiation on a spontaneous mouse mammary adenocarcinoma observed microscopically by means of the transparent chamber technic.

Single doses of radiation, ranging from 2,000 to 5,000 r, were delivered to a small area of the chamber; daily microscopic observations and measurements of the tumor implants were made, and frequent photomicrographs were taken. After a dose of 2,000 or 3,000 r there was marked regression of the implant followed by regrowth. The tumor vessels narrowed, and there was some evidence of a direct action of irradiation on the tumor cells. It was noted that irradiated vessels could not produce new vessels, and that an irradiated bed of tissue was unable to vascularize tumor implants.

The authors conclude that the recovery of tumor cells following irradiation is complete, and that any slowing in the regrowth rate of the tumor was found to be due to vascular abnormalities that developed as a result of the inability of irradiated blood vessel endothelium to grow.

Five sets of serial photomicrographs; 2 graphs; 5 tables

DONALD S. CHILDS, JR., M.D.
The Mayo Clinic

Effect of X-Ray Irradiation on the Alkaline Phosphatase of the Plasma and Tissues of Rats. Stephan Ludewig and Alfred Chanutin, with the technical assistance of Elizabeth Ann Lentz, Ben H. Word, Jr., and J. William Fewell. Am. J. Physiol. **163**: 648–654, December 1950.

The activity of plasma alkaline phosphatase of rats was determined after single and multiple doses of x-rays, at various periods following total body irradiation. Relatively small decreases in phosphatase activity were found after exposure to 300 r. More marked and prolonged decreases were obtained after doses of 500 and 600 r in both fed animals and those deprived of food. Multiple daily irradiation with small doses also caused a decrease in plasma enzyme activity. The alkaline phosphatase activity of the thymus was markedly increased during the first two days following irradiation. Small increases were observed in the spleen. Practically no change in enzyme activity was seen in the liver and kidneys of irradiated rats. The changes in the weights of the thymus, spleen, and liver after irradiation are presented.

Six charts; 1 table.

Effect of Roentgen Rays, Gamma Rays and Beta Rays on the Epidermal Cell. Experiments with the "Nipple-Test" Associated with Dustin's Reaction. W. Jadassohn, E. Bujard, R. Paillard, P. Wenger, and P. Gaudin. Acta radiol. **34**: 469–487, December 1950. (In French)

The authors studied the combined effect of irradiation therapy and treatment by estrogenic hormones on the nipple of the male guinea-pig. Mitotic activity was appraised by means of Dustin's colchicinic reaction.

Application of an estrogen to a normal nipple produces acanthosis, namely a thickening of the epidermis as the result of an increase in the number of cells and a mild degree of simple hypertrophy of those cells. Why increased mitotic activity occurs following application of an estrogen is not understood, but the authors believe that changes in metabolism of the cells lead to simple hypertrophy; hypertrophy proceeds to a certain point, and then mitosis takes place. Thus, the proliferative action compensates for the hypertrophic effect of the estrogen and makes cellular multiplication appear to be the principal factor in production of the acanthosis.

Roentgen, gamma, and beta rays administered in sufficiently large doses inhibit mitosis of epidermal cells of the nipple. Doses of 400 r or more are effective. In spite of the fact that mitosis ceases, the epidermis is thickened, but this is due to an increase in the size of the cells only (pseudo-acanthosis). Doses of 2,400 r were effective in stopping mitosis whether given in single sessions or fractionated. However, if fractionation was stretched to 12 daily doses of 200 r, the effect was not as good. The various types of radiation used (roentgen, gamma, or beta) were equally effective. Following application of an estrogen, a certain number of mitoses do occur, showing that the epidermis still possesses a weak capacity to divide.

The action of estrogen alone differs from the associated action of an estrogen with irradiation in that the estrogen produces simple hypertrophy and favors mitosis. On the other hand, irradiation impairs cellular division in such a way that only the hypertrophic action of the estrogen remains, and pseudo-acanthosis is the result.

Five photomicrographs; 4 tables.

RODERICK L. TONDREAU, M.D.
Lincoln, Nebr.

An Attempt of Excreting Injected Thorotrast in Rabbits by 2,3-Dimercaptopropanol (BAL). Björn E. W. Nordenström-Blomqvist. Acta radiol. **34**: 533–545, December 1950.

The radioactivity of ash of rabbit urine was measured after injection of thorotrast intravenously, 1 ml. per kilogram of body weight. It is believed that the radioactivity measured represented disintegration products of thorium, probably thorium X and mesothorium I. No thorium was present in the urine.

Treatment of thorotrast-injected rabbits with BAL (2,3-dimercaptopropanol) produced no increase in excretion of radioactive elements. Producing acidosis by injection of ammonium chloride in conjunction with BAL injection also failed to increase the excretion of thorium disintegration products. Acidosis is known to promote excretion of lead under BAL therapy.

Studies of residual radioactivity in ashed organs of control and BAL-treated animals showed no appreciable differences between the two. The liver, spleen, kidney, and yellow marrow were checked. The radioactivity of the kidney was low as compared to the liver and spleen.

Measurements were made with commercial Geiger scaling instruments. Autoradiographs were made of urine specimens to determine the type of radiation emanations.

Three roentgenograms; 4 graphs; 3 tables.

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